REMARKS

The subject invention relates to a method of tightening the skin using optical radiation. Claim 15 is the sole remaining independent claim in the application. Claim 15 is directed to the specific preferred embodiment of the subject invention.

As recited in claim 15, the method includes generating a broadband spectrum of near infrared radiation with a filament light source. One example of such a source is a tungsten halogen lamp. A cooled, transmissive material, such as a sapphire window, is placed against the tissue to be treated. Radiation from the source is transmitted through the chilled window to treat the tissue.

In accordance with the subject invention, the treatment period is relatively long, between 1.2 and 5 seconds. In combination with the cooling provided by the transmissive material, an inverted temperature profile is created wherein the temperature in a region below the skin, in the range of about 1 to 5mm, is elevated to at least 50 degrees centigrade. The claimed method produces a noticeable skin tightening which is most likely the result of some form of collagen remodeling.

The assignee herein sells a commercial device under the trademark Titan, which can be used to perform the claimed method. The Titan handpiece includes a tungsten filament halogen lamp which generates broadband, near infrared radiation. This radiation is delivered to the tissue through a chilled sapphire tip.

Applicants have attached as Exhibits A to D copies of articles appearing in various journals which report on investigations using the Titan handpiece. These articles focus on the use of near infrared radiation for skin tightening. All of the articles report positive results. Although it is recognized that surgery may provide better overall results, radiation treatment with the Titan handpiece is advantageous since it is a non-surgical approach with minimal discomfort for the patient.

As noted in the articles, the handpiece generates light primarily in the wavelength range of 1100 to 1800nm which matches the output of the filtered radiation as shown in Figure 5 of the subject application. Although the treatment pulse widths are not expressly discussed in the articles, they can be easily determined. More specifically, the Titan systems used in the treatments described in the articles generates about 16 watts/cm^2 at the output surface of the sapphire window. The articles discuss treatment fluences ranging from 20 to 40 joules/cm^2.

Since one watt delivered for one second creates one joule, a fluence range of 20 to 40 joules/cm^2 would correspond roughly to treatment times of 1.25 seconds to 2.5 seconds, within the limits set forth in the claim 15.

Applicants wish to the note that the studies reported in the attached articles were financially supported by the assignee, as is common when new medical device products are released. It should also be noted that each of these studies were the subject of independent institutional review boards and published in well known journals.

It is respectfully submitted that the particular approach developed by applicants for successfully producing skin tightening is not anticipated or obvious in view of the prior art of record. Applicants have amended claim 15 to more particularly recite the subject method. It is noted that applicants have cancelled claims 45 to 48 which the Examiner rejected as having been dependent on a previously cancelled claim.

Among the references cited by the examiner, the Anderson patent (6,120,497) is arguably the most relevant since it is directed to the concept of treating wrinkles with radiation. As noted by the Examiner, Anderson teaches that it is preferable to heat the tissue to about 50 to 70 degrees centigrade to obtain the appropriate response.

Anderson's principal approach for achieving this goal is completely different from applicants' approach. More specifically, Anderson teaches that it is best to use a pulsed erbium glass laser producing narrowband radiation at 1.54 microns. Further, Anderson teaches that the radiation should be applied in short pulses with a repetition frequency of 4 hertz. Of course, as with most of the prior art to be discussed below, Anderson at least suggests that other light sources, such as incoherent sources, can be used such. However, Anderson does not disclose applying long pulses of radiation from a broadband near infrared source.

The two other references cited by the Examiner are both lengthy, relatively generic patent publications to Altshuler (2004/0093042 and 2002/1073780). These publications describe using all manner of radiation sources, to treat a vast array of various maladies using a wide variety of different treatment parameters. As will be discussed below, it is improper for the Examiner to rely on these generic disclosures to conclude that applicants' specific and successful approach for skin tightening is obvious.

Turning first to Altshuler '042, the Examiner is correct that he discloses virtually every type of light source for treatment purposes. Altshuler '042 also includes an impressive laundry

list of possible treatments. However, Altshuler '042 provides no specific teaching that would directly address applicants' narrow and specific embodiment. For example, Altshuler suggests that the treatment time can range from 2 seconds to 2 hours. Further examples of treatment times in his Tables are in the form of broad ranges. Altshuler '042 fails to teach or suggest using broadband near infrared light from a filament lamp applied for a period of between 1.2 to 5 seconds to tighten the tissue.

Applicants acknowledge that Altshuler's broad time ranges overlap the claimed range of 1.2 to 5 seconds. However, that alone is not determinative of patentability (see MPEP 2131.03 and 2144.05). As can be seen in the attached articles, it has been demonstrated that the narrow range of 1.2 to 5 seconds set forth in claim 15 is best suited for tissue shrinkage when combined with broadband near infrared radiation from a filament light source. On this issue, the Examiner is again reminded that the teachings of the Anderson patent, which is also directed to skin tightening, primarily teaches using a narrowband laser and short pulses. It is respectfully submitted that in context of all the prior art, it is unfair to argue that the broad and unrestricted disclosures in Altshuler '042 are sufficient to teach to one skilled in the art the specific claimed method developed by the applicants.

In the Office Action, the Examiner cited Altshuler '780 for its teaching of cooling after treatment with the radiation. It is respectfully submitted that Altshuler '780, which is primarily directed to using a waveguide for channeling light from a light source to the tissue, is no more relevant than Altshuler '042, in teaching or rendering obvious applicants' invention.

In summary, it is respectfully submitted that applicants have developed a very specific and successful approach for tightening the skin. Applicants have submitted a claim directed to this specific embodiment. While it is possible for the Examiner to find bits and pieces of this method in the prior art, when taken as a whole, those teachings would not have led one skilled in the art to applicants' method. For this reason, it is believed that the invention as recited in amended claim 15 defines patentable subject matter and allowance thereof is respectfully requested.

Respectfully submitted,

STALLMAN & POLLOCK LLP

Dated: September 15, 2008

By: _____
Michael A. Stallman (Reg. No. 29,444)

Attorneys for Applicant(s)

EXHIBIT A

Journal of Cosmetic and Laser Therapy. 2007; 9: 35–40

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healthcare

ORIGINAL ARTICLE

Treatment of skin laxity of the lower face and neck in older individuals with a broad-spectrum infrared light device

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Abstract

Background: Non-ablative approaches with infrared and radiofrequency energy sources have been shown to reduce skin laxity, but studies have focused on individuals with early-stage, mild-to-moderate degenerative dermal changes. *Objective*: The purpose of this prospective study was to evaluate the safety and efficacy of an infrared light device for the treatment of skin laxity in patients with soft tissue ptosis of the lower face and neck characteristic of the sixth decade of life and beyond. *Materials and methods*: Thirteen females, aged 58–83 years old (average: 64 years), were treated with a filtered 1100–1800 nm infrared light-based device. All individuals presented with ptotic soft tissue, but varied in the extent of skin laxity from no visible laxity to having pendulous excess skin. Two treatment sessions were provided at monthly intervals. The individuals returned for follow-up visits at 1, 3 and 6 months after the second treatment. Twelve of the individuals completed the study. *Results*: Changes were dramatic for those individuals in whom the skin envelope appeared to drape separately from deeper soft tissue. No treatment complications were noted. *Conclusion*: Infrared light source-induced skin tightening may be induced even in older individuals.

Key words: *skin laxity, infrared light, cosmetic treatments of the neck*

Introduction

Aesthetic re-contouring of the aging neck has traditionally entailed surgical procedures. However, surgery can preclude individuals for whom it is not medically advisable or personally desirable. Non-ablative approaches with infrared and radiofrequency energy sources have been shown to reduce skin laxity, but studies have focused on individuals with early-stage, mild-to-moderate degenerative dermal changes. It has anecdotally been suggested that patients in their sixth and later decades of life may not be the best candidates for non-invasive skin tightening.

The purpose of this prospective study was to evaluate the safety and efficacy of an infrared light device for the treatment of skin laxity in patients with soft tissue ptosis of the lower face and neck characteristic of the sixth decade of life and beyond.

Figure 1. A 66-year-old female with soft tissue settlement in the jowls but with no apparent excess of skin.

Materials and methods

Thirteen females, aged 58–83 years old (average: 64 years), were treated with a filtered infrared light-based device (Titan, Cutera, Brisbane, CA, USA). The device provides dermal heating by delivering infrared light in the 1100–1800 nm wavelength range, which is absorbed by water in

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(Received 20 November 2006; accepted 24 December 2006)

ISSN 1476-4172 print/ISSN 1476-4180 online © 2007 Taylor & Francis
DOI: 10.1080/14764170601186107

Figure 2. A 70-year-old female with loose, excess skin on the neck and fat accumulation on the face and neck.

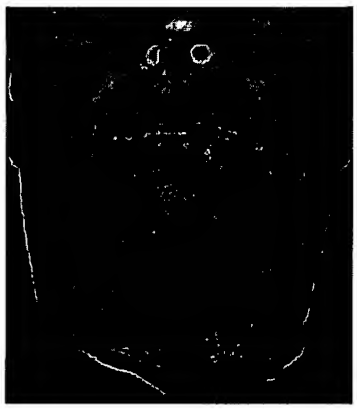
the skin. Energy is delivered with a spot size of 1.5×1 cm and pulse durations of up to 11 seconds.

All individuals presented with ptotic soft tissue, but varied in the extent of skin laxity from no visible laxity to having pendulous excess skin. They also varied in the amount of surplus fat from having no extra fat to having extensive, weighty fat deposits (Figures 1–3).

The study was undertaken under the auspices of the Institutional Review Board of Pascack Valley Hospital, Westwood, NJ, USA. All individuals received applicable informed consent. Standardized photography was utilized. All treatments were performed by one physician (AF). Treatment areas extended from the nasolabial fold to the preauricular area and from the malar prominence to the clavicle. Prior to treatment, a layer of ultrasound gel, approximately 1 mm thick, was applied to the area to be treated. Three passes of adjacent pulses were applied, with each pulse covering an area of 1.5 cm^2. The average number of pulses applied per session was 312 (range: 230–440). Fluence was set to 36 J/cm^2 for the majority of the pulses and adjusted based on patient comfort (range: 30–36 J/cm^2). Pre-, parallel, and post-cooling of the epidermis to under 40°C was accomplished through continuous contact with a sapphire tip.

Additional gel was applied as needed during the treatment session. Each individual received two treatments spaced 1 month apart. The individuals returned 1, 3 and 6 months after the second treatment for photographic documentation and follow-up evaluation.

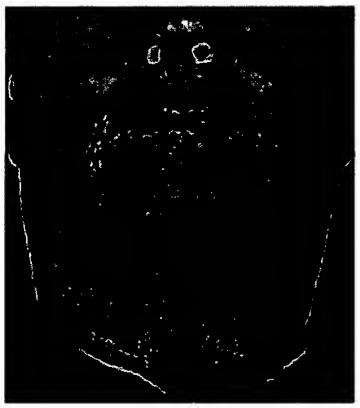
Clinical evaluations were undertaken by the treating physician. Another non-treating physician



(A)

(B)

Figure 3. (A) A 64-year-old female with a large volume of excess skin on the lower face and neck; (B) Subject with a large volume of excess skin on the lower face and neck (sideview of subject shown in Figure 3a).



(A)

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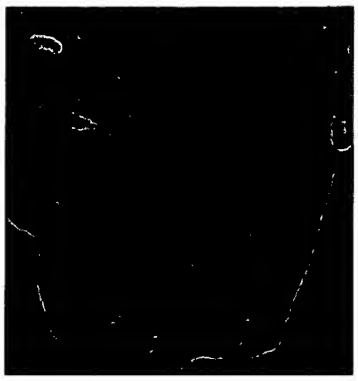
Figure 4. (A) A 64-year-old female before treatment; (B) 6 months after two treatments. Note the tightening of the jawline and neck.

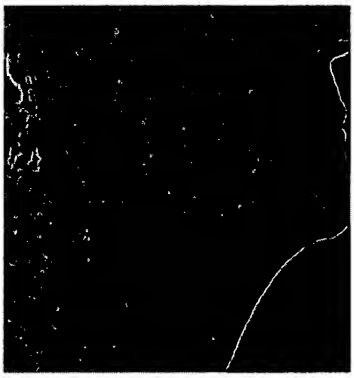


(A)

(B)

Figure 5. (A) Same individual as in Figure 4 before treatment; (B) 6 months after two treatments.

(A)



(B)

Figure 6. (A) A 64-year-old female before treatment; (B) 6 months after two treatments.

(DJG) undertook independent analysis of unlabeled digital photographs.

Results

All treatments were well tolerated without the use of oral medications or topical anesthesia. Mild, transient erythema was the only side effect noted; no blisters or burns occurred. Erythema was seen with all individuals immediately after treatment and typically resolved within 30 minutes.

Twelve out of 13 individuals kept all study visits. One individual was lost to follow-up. Clinically obvious improvement was seen in 11 of 12 individuals.

Changes were dramatic for those individuals in whom the skin envelope appeared to drape separately from deeper soft tissue (Figures 4–9). The noted changes consisted of improved mandibular definition, increased cervicomental angularity, and decreased redundancy in neck skin and/or slimming of the neck contour. Clinically observed changes coincided with those seen by the non-treating independent observer.

In those individuals in whom the skin had descended but stayed largely intact with the subcutaneous tissue, improvement was mild to moderate (Figure 10). The one individual gaining no noticeable improvement presented with jowls formed by fat descent but no excess skin (Figure 1). Individuals continued to improve past the 1-month follow-up visit (Figures 11–13). No scars or pigmentary alteration was noted.

Discussion

As non-invasive, non-ablative rejuvenation techniques have become more popular, non-surgical skin tightening has become another frontier in aesthetic medicine. Non-ablative monopolar radiofrequency has been successfully used for this purpose (1–4) and, until recently, has been the only such technology available on the market. Unfortunately, because of initially used high fluences that were associated with a significant delayed clinical response, and the potential risk of rare fat necrosis and scarring, other approaches have also been considered. This study utilized a new infrared device that delivers light with wavelengths between 1100 and 1800 nm, targeting water and resulting in collagen denaturation and dermal tightening.

Collagens are triple helices of polypeptide chains, held together by hydrogen bonds. As collagen is

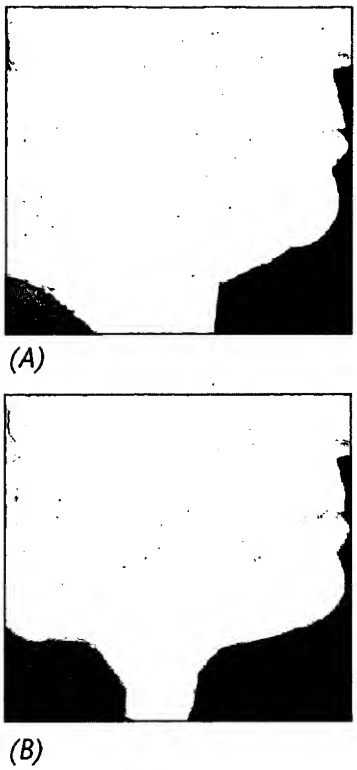


Figure 7. (A) A 61-year-old female before treatment; (B) 6 months after two treatments. Note the improvement in mandibular definition and the cervicomandibular angle.

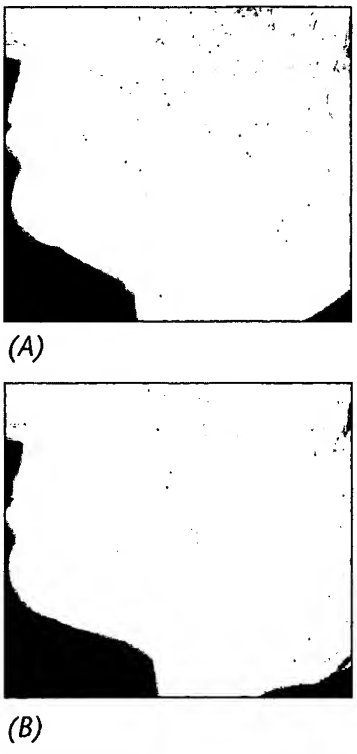


Figure 8. (A) Same individual as in Figure 7 before treatment; (B) 6 months after two treatments.

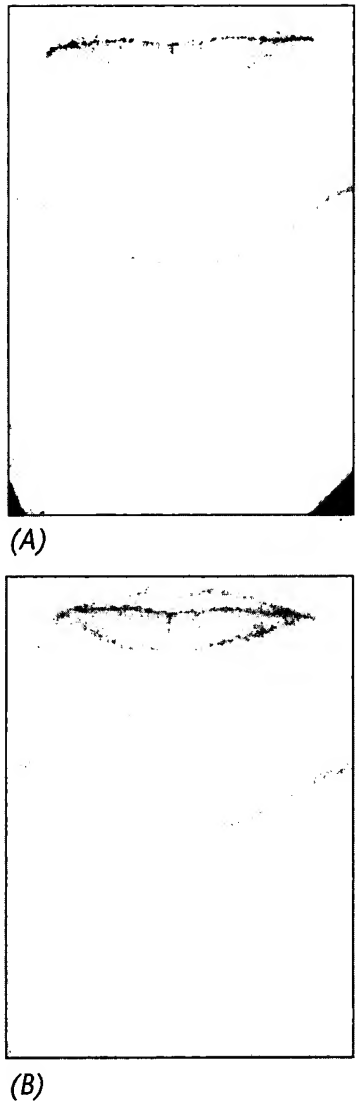


Figure 9. (A) A 61-year-old before treatment; (B) 6 months after two treatments.

heated it undergoes denaturation. This process is not completely understood, but is thought to involve breakage of hydrogen bonds and a conversion from a crystalline to an amorphous state (5). This results in thickening and shortening of collagen fibrils, increased tissue tension due to the rubber-elastic properties of collagen, and, ultimately, tissue tightening (6). Higher heating temperatures, however, may be associated with liquefaction of collagen and other dermal proteins, with the resulting inability to contract and a subsequent healing process akin to scarring.

Various in vitro studies on mammalian skin suggest a thermal denaturation temperature of between 58°C and 68°C (7). More recent research suggests that collagen denaturation does not occur at a specific temperature, but rather follows a

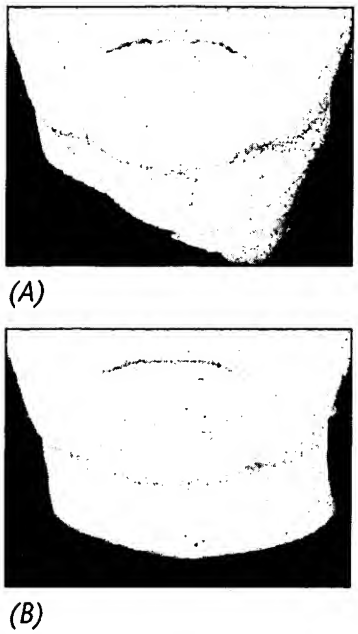


Figure 10. (A) A 70-year-old female before treatment; (B) 6 months after two treatments. Improvement was limited by submental fat distribution.

mathematical construct known as the Arrhenius equation. According to this equation, for every 5°C decrease in temperature, a 10-fold increase in treatment duration is needed to achieve the same amount of denaturation of collagen (6). Thus, a combination of temperature and time, rather than time alone, determines the amount of collagen denaturation and tissue contraction.

Dermal water is a convenient heating tissue target, as it allows for an even distribution of heat in the treatment zone. The infrared device used in this study features a large spot size (1.5 × 1 cm) and long pulse durations of up to 11 seconds. The depth of heat penetration is estimated to be 1–2 mm, with some heat reaching as deep as 5 mm (8).

Because of long pulse durations, much lower fluences can be utilized with the chosen light-based device. This results in minimal discomfort. In a recent study, fluences as low as 20–30 J/cm^2 were used, precluding the need for topical anesthesia (8).

Few studies have so far evaluated the skin tightening clinical efficacy of broad-based infrared heating. In a previous study of 25 individuals, 22 experienced immediate contraction, with the persistence of clinical improvement for up to 12 months. Of note, fluences of 30 J/cm^2 in combination with 150–360 delivered pulses produced better clinical results when compared with fluences of 20 J/cm^2 with less than 150 pulses. Additionally, eight out of nine individuals in this previous study had previously been treated with a non-ablative radiofrequency device and reported equal or superior results with infrared studies (8). It should, however, also be noted that an earlier report failed to demonstrate such results (9). However, different treatment parameters were used in these studies. Recent ultrastructural analyses confirm that the degree of collagen fibril alteration was fluence-dependent with this selectively filtered infrared device. This, at least in part, may explain the differing results (10).

What remains unclear is why some treated individuals respond well to treatment, while others may not. In our non-responsive individuals, infrared heating may have contracted the lax skin, but the degree of visual impact was constrained by the small amount of excess skin relative to the underlying structure and/or the resistance of dense fat deposition.

This study is the first to show that non-surgical tightening of neck and jowl skin may be produced in an older population. The study also confirms the safety and efficacy of infrared light-based heating in

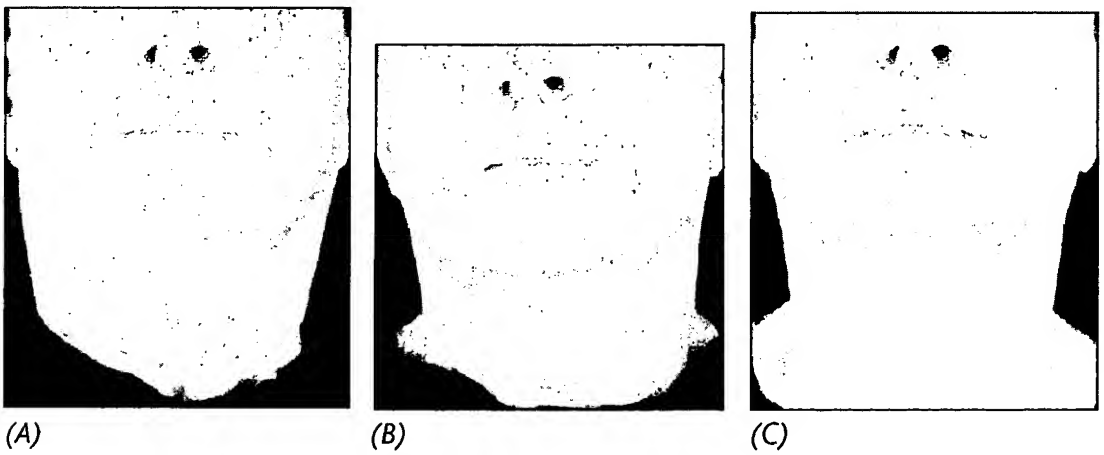


Figure 11. (A) A 64-year-old female before treatment; (B) 3 months after two treatments; (C) 6 months after two treatments. Note the continued improvement from 3 to 6 months after treatment.

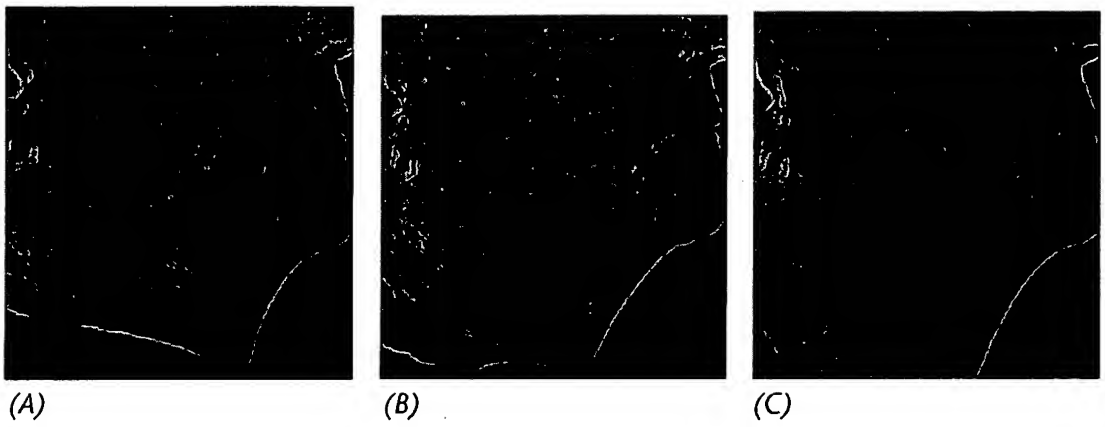


Figure 12. (A) Same individual as Figure 11 before treatment; (B) 3 months after two treatments; (C) 6 months after two treatments. Note the continued improvement from 3 to 6 months after treatment.

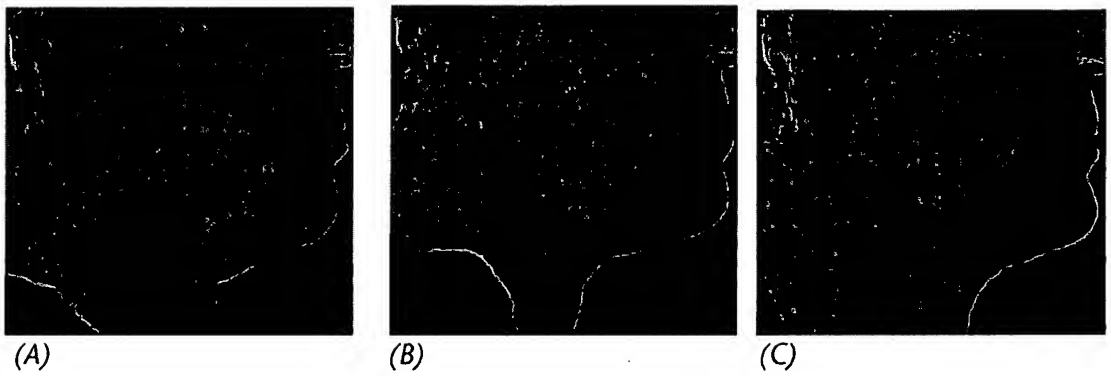


Figure 13. (A) A 61-year-old female before treatment; (B) 3 months after two treatments; (C) 6 months after two treatments. Note the continued improvement from 3 to 6 months after treatment.

the reduction of skin laxity. While the impact of non-ablative dermal tightening can be modest compared to surgical results, significant improvement in submental and submandibular definition can be accomplished. Improvement was most dramatic in those for whom loss of definition was due, at least in part, to excess skin that suspended beyond underlying structures. This study, small in size, was meant as a pilot trial. Larger series of treated individuals are required for a more detailed statistical analysis of our findings.

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EXHIBIT B

Near Painless, Nonablative, Immediate Skin Contraction Induced by Low-Fluence Irradiation with New Infrared Device: A Report of 25 Patients

JAVIER RUIZ-ESPARZA, MD

BACKGROUND Nonablative radiofrequency (NARF) has been the only method for producing noninvasive skin tightening. Nevertheless, significant pain during the procedure is an important downside of this technology. A new nonablative medical device, Titan (Cutera, Inc., Brisbane, CA, USA), capable of fluences much lower than those possible with NARF, was tested as a less painful alternative.

OBJECTIVES To produce skin contraction leading to lifting of eyebrows and/or improvement of lower face and neck skin laxity using fluences below pain levels.

PATIENTS AND METHODS Twenty-five patients were treated. Standardized photographs were obtained preoperatively, after a few days, a few weeks, and up to 12 months after the procedure.

RESULTS Immediate changes were obtained in 22 of 25 patients. Examination of photographs revealed that the initial improvement was maintained throughout the follow-up period.

CONCLUSION Immediate true skin contraction persisting through the immediate, intermediate, and long-term follow-up was found in the vast majority of patients in this group. Edema as an artifact simulating immediate improvement was excluded by serial photographs taken during the follow-up period. Skin contraction occurred at low fluences, below the threshold of pain. This, to the best of our knowledge, has not been previously described in the medical literature.

Cutera, Inc. loaned the Titan infrared device used in this study.

Noninvasive, nonablative, no down-time methods of rejuvenation for the face and neck have surpassed ablative methods in public demand. Intense pulsed light is used for improving skin texture, dyspigmentation, and telangiectasia.[1,2] Recent developments in the treatment of telangiectasia using lasers have been reported.[3,4] Nonablative radiofrequency (NARF) has been a recent addition to this armamentarium. It has been shown to produce skin tightening, which is beneficial in the cosmetic appearance of the face and neck.[5–13] Until now, it has been the only technology that has produced skin tightening noninvasively. However, pain and delayed clinical response in the vast majority of patients remain two significant factors in the use of this method. High fluences (70–150 J/cm^2) delivered in a short fixed pulse (2.3 seconds or less) are typical NARF ThermaCool system (ThermaCool, Thermage, Hayward, CA, USA) treatment parameters. Pain is significant even at the lowest possible fluence capabilities of that machine as heat is delivered in an extremely short pulse (flash heating). Multiple passes over a small area will eventually produce edema, which will give the transient illusion of improvement. This edema is seen immediately after the procedure but will disappear in the intermediate follow-up period (3–14

University of California, San Diego, California

 • Published by Blackwell Publishing • ISSN: 1076-0512 • Dermatol Surg 2006;32:601–610 • DOI: 10.1111/j.1524-4725.2006.32130.x

days). On the other hand, targeting such change as an end point of the procedure may prove risky regarding late-appearing complications such as fat necrosis and subcutaneous scarring.

Our use of a novel medical infrared light device emitting light at 1,100 to 1,800 nm in multisecond cycles is described in this report. At these wavelengths, this device has a moderate level of water absorption, and, therefore, it can thoroughly heat the dermis over a period of seconds. It differs from currently available infrared devices in that they usually have much smaller spot sizes and also have very short pulse durations (milliseconds) as well as a very high water absorption, which results in shallow heating only. In contrast, this new device has a large spot area (1 cm × 1.5 cm). Although it is an infrared lamp, it is not a flashlamp. Flashlamps produce light at lower wavelengths (more visible light) and are usually pulsed at short (millisecond) durations. Titan has a broadband infrared lamp that emits longer wavelengths and is better suited for multisecond pulse durations. Heat penetration depth from this device is estimated to be about 1 to 2 mm, but some heating does occur down to about 5 mm. These calculations were carried out using dermal scattering coefficients and water penetration depths for near-infrared wavelengths to estimate an effective penetration depth for a particular wavelength. The total intensity was then calculated by adding up the contribution from individual wavelengths. These models were then confirmed by actual thermal measurements of ex vivo tissue samples, and an appropriate filter design was selected based on the desired thermal profile obtained.

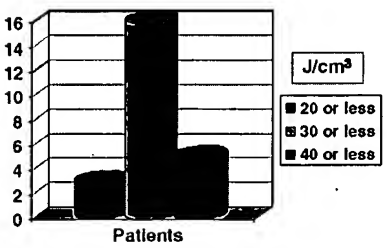

Figure 1. Fluences used in the study.

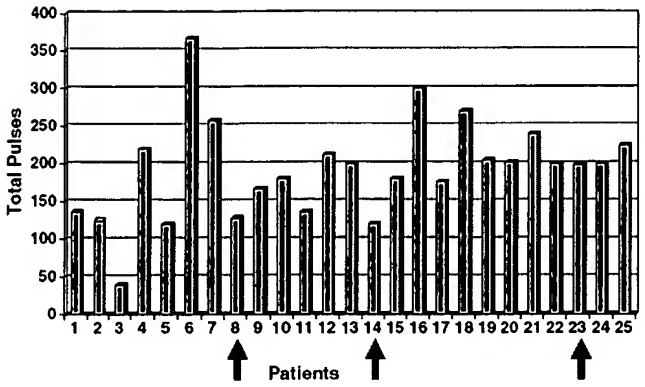

Figure 2. Total number of pulses per treatment per patient. The red arrows show the patients with no response.

This device has pre-, parallel-, and post-cooling and delivers up to 50 J/cm^2 in pulse duration of up to 8.1 seconds. Because of a much longer pulse and much lower energies (20–30 J/cm^2) as used for the vast majority (19 of 25) of patients in this report, the degree of pain is considerably less and much better accepted by patients. In addition, immediate results were seen in 22 of the 25 subjects treated in this study, suggesting a different mechanism of action, i.e., immediate collagen contraction.

Patients and Methods

A novel medical device named Titan (Cutera, Inc., Brisbane, CA, USA) was used for these treatments. This device heats the dermis using an infrared light source with a wavelength range between 1,100 and 1,800 nm. It provides contact cooling through a sapphire window. This allows for pre-, parallel-, and post-cooling, which allows infrared light to heat the treated tissue without epidermal ablation.

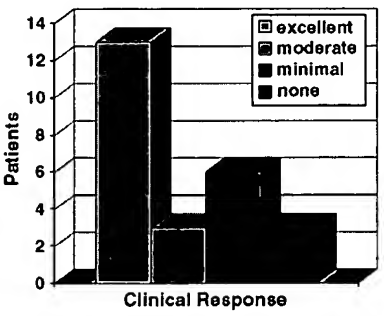

Figure 3. Results: Degree of clinical improvement in 22 of the 25 patients in this study.

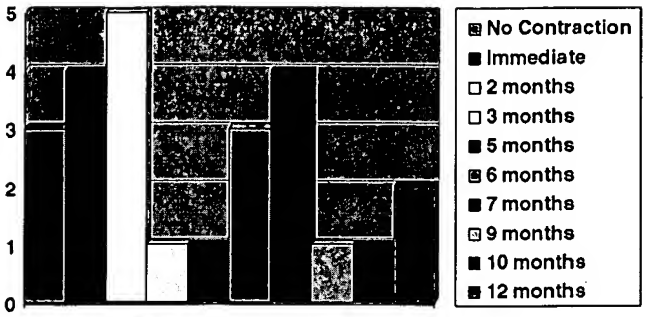

Figure 4. Permanence of skin contraction. Three of 25 patients had none. Twenty-two had immediate contraction. In four patients, only immediate follow-up was available. In all others, contraction was seen both in the immediate follow-up period and up to 12 months.

TABLE 1. Comparison Results in Nine Patients who were Treated with Both Modalities

Results	*None*	*Minimal*	*Moderate*	*Excellent*
Titan	1	3	1	4
ThermaCool	4	4	0	1

It has a large 10 × 15 mm delivery area. The target chromophore is water. It has a pulse duration of up to 8.1 seconds.

A group of 25 patients, two men and 23 women ranging from 44 to 75 years of age, skin types I to V, were treated for facial rejuvenation using the new infrared light device. They were treated for eyebrow lifting only ($n = 3$), eyebrow lifting as well as cheek and neck skin flaccidity ($n = 21$), and lower face only ($n = 1$). Twenty patients had a single treatment session while four had two sessions and one had a total of three sessions. Treatments were performed at fluences ranging from 20 to 40 J/cm^2 (Figure 1). On the forehead, only focal areas were treated according to the principle of anchoring points previously described (5), while on the cheeks, the flaccid areas of the jowls and lower cheeks were treated directly. The total number of pulses for treating these areas in these patients is shown in Figure 2.

Figure 5. Schematic diagram demonstrating the heat shrinkage of collagen from a structured triple helix to a random coil structure.

All patients were informed of the off-label use of this FDA-approved device. Each signed an operative permit after being informed of the experimental nature of the procedure. They were directed to wash their face in our office with soap and water three times to remove any possible cosmetic residues. Preoperative photographs using a high-resolution digital camera (Epson Photo PC 3000Z, Epson America Inc., Long Beach, CA, USA), room lighting, distance, and position of the patient were standardized. The areas to be treated were marked with an eyebrow pencil. The marked areas were then treated with the infrared light device, making sure that protective metal goggles were being used by the patient and adequate operating goggles by the medical staff. After the procedure, the patient washed his or her face again, and photographs were taken while the preoperative photographs were being displayed in a computer monitor for the photographer to match the positioning of the patient as closely as possible. Patient satisfaction after their self-observation in the mirror was obtained. Two possible grades of satisfaction were given: happy or not happy with results. Photographic comparison of pre- and immediate postoperative material was used to evaluate the results objectively. Photographic material was evaluated blindly by

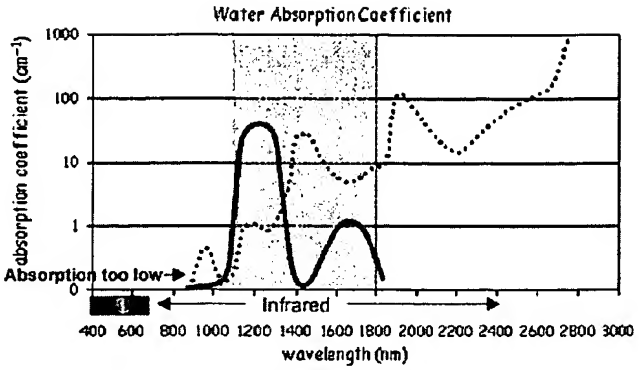

Figure 6. Spectrum of the absorption coefficient of water. Wavelengths in the range from 1,100 to 1,800 nm provide a penetration depth of 1 to 2 mm, assuming that the strongly absorbed wavelengths in the range from 1,400 to 1,500 nm are attenuated.

an individual independent to the study and graded in a quartile grading system as excellent, moderate, minimal, or no improvement. Excellent was defined as an overall change in all treated areas. Moderate was focal changes in all treated areas. Minimal was focal changes only, and none was when no changes at all were seen. Standardized follow-up pictures from the immediate postoperative period and up to 12 months were obtained in all patients.

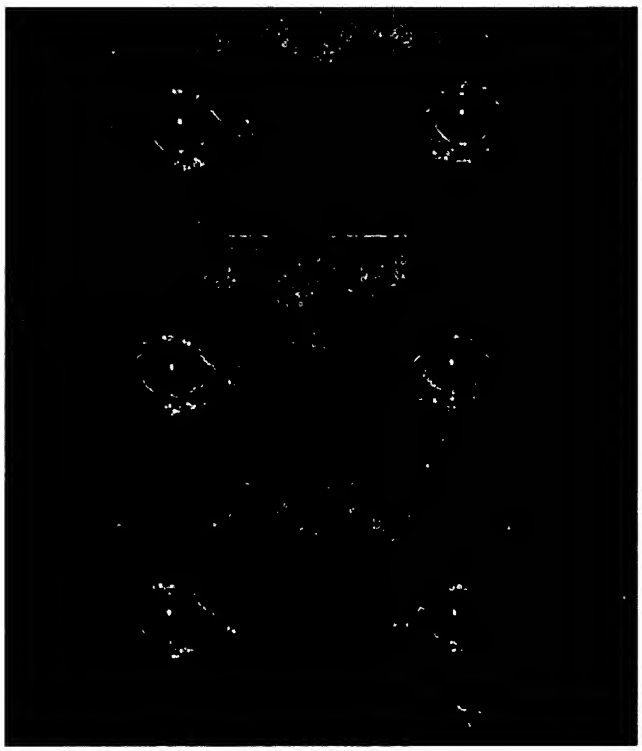

Figure 7. Eyebrow lift in a 44-year-old man. From top to bottom: pretreatment, immediately after first treatment, and immediately after second treatment. No anesthesia, no pain.

Nine of our patients had had treatment with NARF using the ThermaCool system before their treatment with infrared light, which gave us an opportunity to compare results from both treatments.

Results

Review of photographs revealed demonstrable changes in 22 ($n = 22$) of 25 patients in at least one of the areas treated. Eyebrow lifting as well as skin laxity improvement were observed. Immediate results were seen in 22 of 25 patients. In this study, fluences ranging from 20 to 30 J/cm^3 were used for the majority of patients ($n = 20$), while 40 J/cm^3 was used in the other five. A fluence of 20 J/cm^3 has a delivery time of 5.3 seconds and 30 J/cm^2 has a delivery time of 6.2 seconds in total, which includes pre- and post-cooling times (1 and 2 seconds, respectively). In two patients, fluences of 40 J/cm^2 were used for eyebrow lifting. No change was observed at these energy levels; they both responded later to 20 J/cm^3. The first two patients treated gave us the indication that the lower fluences could be tolerated well without a topical anesthetic; however, the first five were still treated using a topical anesthetic. Subsequent treatments were applied without any anesthetic at all. Patients were comfortable throughout the treatment and mentioned no pain at all at levels of 30 J/cm^3 and below. Of the 24 patients treated for eyebrow lifting, six failed to show any change.

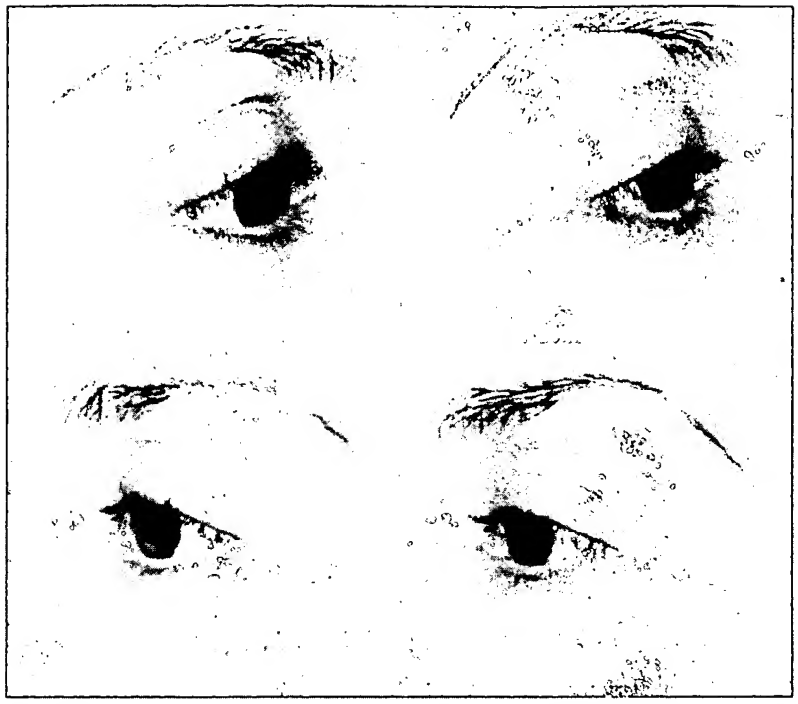

Figure 8. Immediate eyebrow lift: note change in the shape of the arch of eyebrow as well as decreasing skin folds in upper lids from eyebrow elevation in a 48-year-old woman 20 J/cm^2 27 pulses (upper and lower left: preoperative, upper and lower right: immediate). No anesthesia was used, and no pain was felt.

Of the 22 patients who received treatment for cheek and neck flaccidity, four failed to respond. In three patients, no changes were seen in any of the areas treated. No difference in the degree of response was seen related to age, sex, or skin type. Excellent results were seen in 13 patients, moderate in three, minimal in six, and no results at all in three (Figure 3). Two subgroups can be considered in evaluating fluence with number of pulses as they related to clinical response: in the first group (seven patients) very low fluences (20–25 J/cm^3) with very low number of pulses (below 150) were used, and in the second group (18 patients) fluences of 30 J/cm^3 combined with a high number of pulses (150–360) were used. The first group rendered minimal or no response, while the second group consistently yielded moderate to excellent results. Immediate skin contraction was seen in 22 patients. Photographs taken a few days later demonstrated permanence of results, excluding the possibility of edema as an artifact. Interestingly, in two of the nonresponders, no contraction was seen in six and seven follow-up periods, respectively. The third nonresponder did not return for follow-up. In all the cases that demonstrated immediate changes, the contraction persisted throughout a follow-up period of up to 12 months (Figure 4). In no instance did the initial contraction disappear during follow-up.

The relation between immediate contraction and long-term contraction in these patients is also shown in Figure 4.

In the nine patients studied who had been treated with the ThermaCool device before their treatment with Titan, the latter gave equal or superior results in eight patients. In only one case was ThermaCool better (Table 1).

Isolated small, superficial second-degree burns were seen in three patients in single areas for each patient; they healed uneventfully. No other complications and no pre- or postoperative care were needed except for minimal local care for the three patients with the small burns. All patients returned to their normal activities immediately, including the patients who developed small focal burns. All patients expressed satisfaction with the procedure.

Discussion

Collagen is a family of structural proteins, creating strength and resilience in the skin and other tissues. Collagen fibers are composed of a triple helix of protein chains, with interchain bonds creating a crystalline structure for the collagen. While most of the laboratory studies on collagen shrinkage or denaturation have been performed ex vivo, these studies have shown that heated collagen transforms from the crystalline triple helical structure to an amorphous, random-coil structure through the breakage of the hydrogen bonds linking the protein

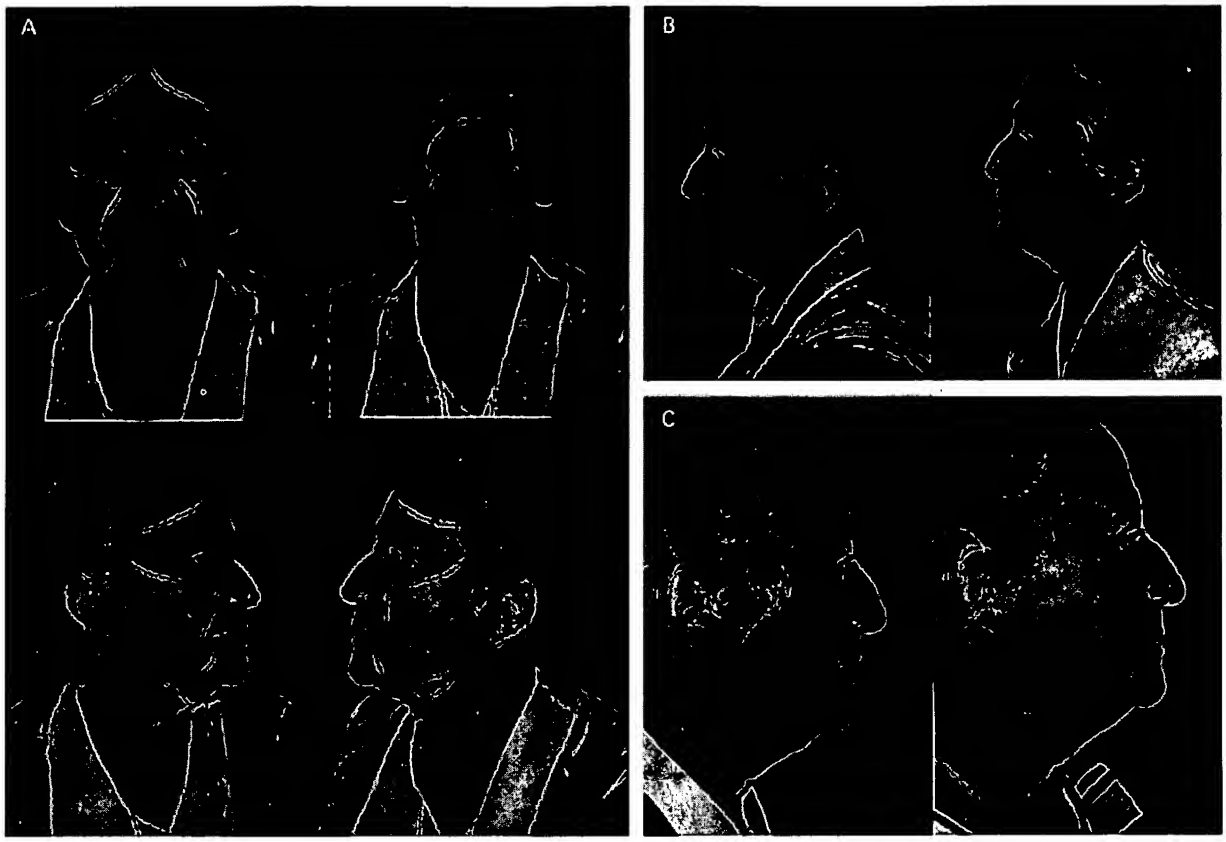

Figure 9. (A) Typical areas of treatment. The areas were delineated with an eyebrow pencil after the patient washed her face thoroughly. (B) A 74-year-old woman. One treatment session. Before and immediately after. 30 J/cm^2 144 pulses to cheeks and neck. 80 pulses to temples. Notice eyebrow-lifting effect and lower cheek and jowl as well as neck improvement. (C) Opposite side on the same patient 9 months after a single treatment. Notice continued improvement.

strands of the triple helix.[14] This creates a thickening and shortening of the collagen fibers as the chains fold and assume a more stable configuration, as shown schematically in Figure 5. This immediate collagen contraction can be used for cosmetic treatments to treat skin laxity or other signs of aging on the face or the body.

Until now, tightening lax skin in a noninvasive way needed the use of NARF. Its application was painful, and the results generally needed 3 to 6 months to show. Immediate changes are said to occur, but serial photographs during the immediate and midrange follow-up to exclude edema as the cause of the improvement have not been reported. For the first time, an alternative source of energy used for the purpose of skin tightening, infrared light, is described. It produces skin contraction in a nonablative form, but in contrast with the NARF device, it does so in a virtually painless manner and with immediate demonstrable changes in 22 ($n=22$) of the 25 patients treated in this study. The probable reason for comparatively much less pain with the new infrared light device is its multisecond pulse width as well as the low fluences used in this study.

A temperature of 57 to 61°C is often quoted as the shrinkage temperature of collagen. However, a more complete analysis shows that collagen contraction is a rate process characterized by the Arrhenius equation.[15] The general form of the Arrhenius equation is given by

$$k = A^* \exp^{(-E_a/R^*T)}$$

where k is the rate, E_a is the activation energy for the process, and T is the temperature (in Kelvin). Based on assumed parameters for collagen in general, this equation shows that for every 5°C decrease in temperature, a 10-fold

Figure 10. A 55-year-old woman demonstrating immediate and sustained improvement on jowl and neck areas visible from the immediate postoperative period and still present after 12 days.

increase in time is needed to achieve a similar amount of collagen contraction.[15] Thus, no single shrinkage temperature exists, and the amount of collagen contraction is determined by a combination of the time and temperature. Studies suggest that for millisecond domain exposures, the shrinkage temperature is above 85°C, while for relatively long exposures of several seconds, the shrinkage temperature is in the range of 60 to 65°C.[15,16] At present, it is completely unclear whether controlled collagen denaturation/thermocontraction can be made to occur before significant cellular damage occurs.

While no definitive study has shown what the ideal depth is to treat skin laxity through collagen contraction, heating to a depth of 1 to 2 mm targets the dermal collagen fibers while allowing a cooling mechanism to protect the epidermis. Light can be used to provide the desired heating at this depth through a proper selection of an absorption target (chromophore) and wavelengths. Water provides an ideal absorption target to create an even distribution of heat in the treatment volume. Figure 6 shows the absorption curve for water. Wavelengths in the range from 1,100 to 1,800 nm have an appropriate penetration depth but require the attenuation of the strongly absorbed wavelengths in the range from 1,400 to 1,500 nm.

This new device has been designed based on the theory of collagen contraction. Water was chosen as the target chromophore, allowing uniform heating of the targeted volume. A tailored spectrum from 1,100 to 1,800 nm allows a penetration depth of 1 to 2 mm, ideal for targeting the reticular dermis. This tailored spectrum includes filtering of the strongly absorbed wavelengths in the 1,400 to 1,500 nm range. A multisecond exposure is used with sufficient energy to create the desired combination of time and temperature for collagen contraction. The epidermis is protected through continuous contact cooling.

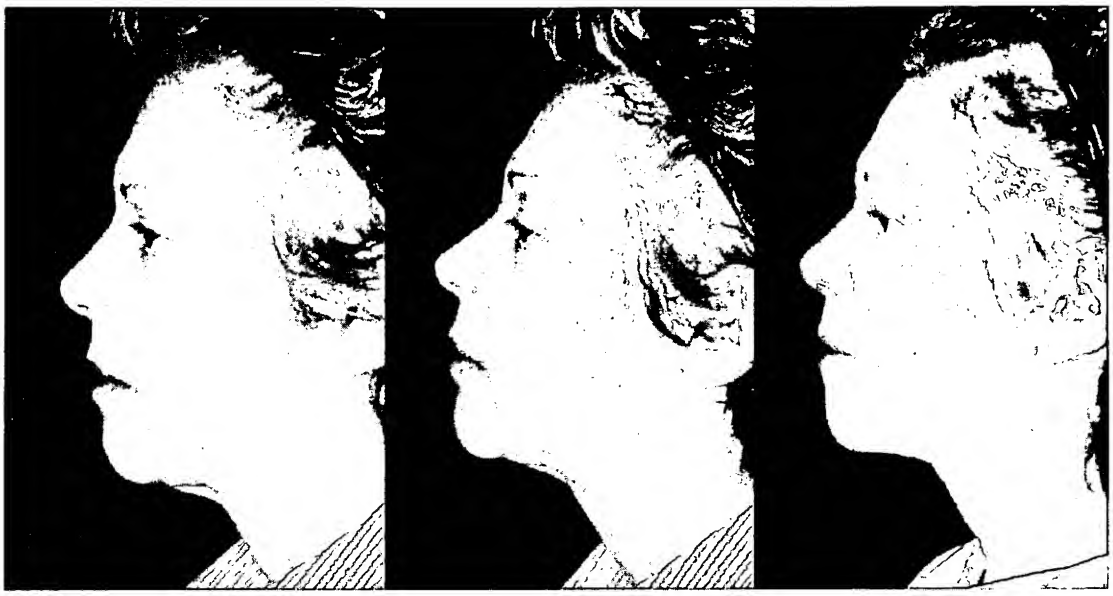

Figure 11. A 65-year-old woman showing gradual improvement in eyebrow position, nasolabial fold, cheek, and neck skin. Shown preoperatively, immediately after the procedure, and 8 weeks later (from left to right, respectively).

The photo sequences in Figures 7–15 demonstrate immediate collagen contraction using the unique combination of treatment parameters found in this new device. Figures 7 and 9–15 show permanence and progression of the immediate changes into the earliest and midrange follow-up periods. When examining claims of immediate collagen contraction, it is important to distinguish edema caused by treatment from actual skin tightening. Edema can temporarily improve the cosmetic appearance of a patient by smoothing rhytids, but this will disappear within a few days. In addition, in the neck, especially in the submental area, any change caused by edema would worsen the appearance due to swelling under the chin. Only true skin tightening would make it look

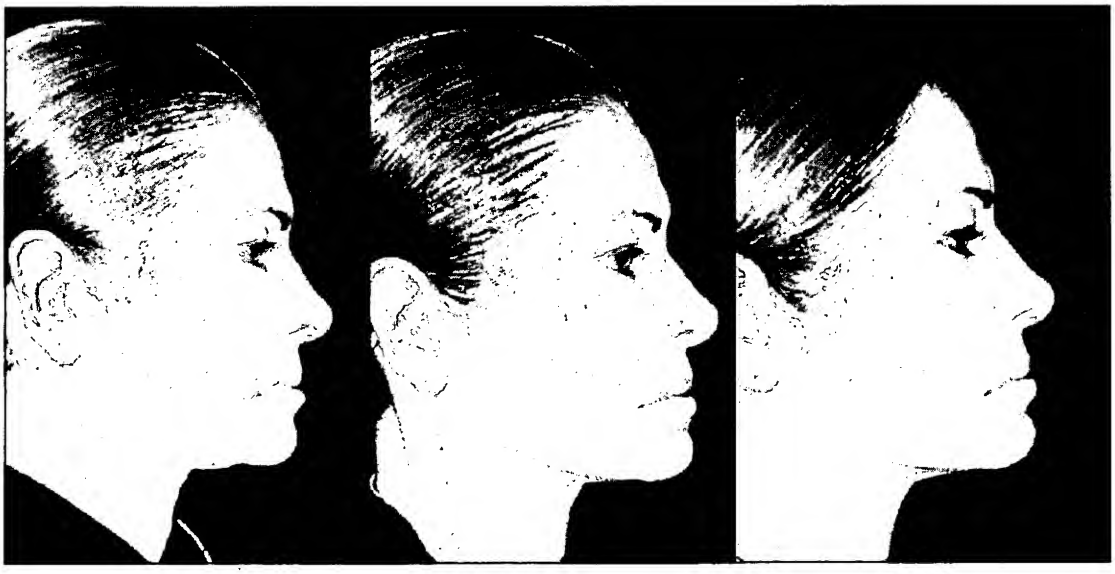

Figure 12. A 44-year-old woman preoperatively (left), immediately after (center), and 10 days later (right) showing that the immediate improvement of lower face and neck is maintained after 10 days.

Figure 13. (A) A 59-year-old woman. Four months after her second Thermage treatment and immediately pre-Titan. (B) Immediately post-Titan. Dramatic immediate tightening. (C) Seven months after a single Titan treatment. The improvement seen immediately has been maintained after 7 months.

better. The same is true for eyebrow lifting; any degree of edema would cause increased weight and bulk on the eyebrow line, lowering and not raising them. Our patients' photos demonstrate immediate collagen contraction on the submental area, and similar immediate changes due to collagen contraction are demonstrated on the eyebrows and cheeks. The fact that the changes were sustained and even improved over time attests to this.

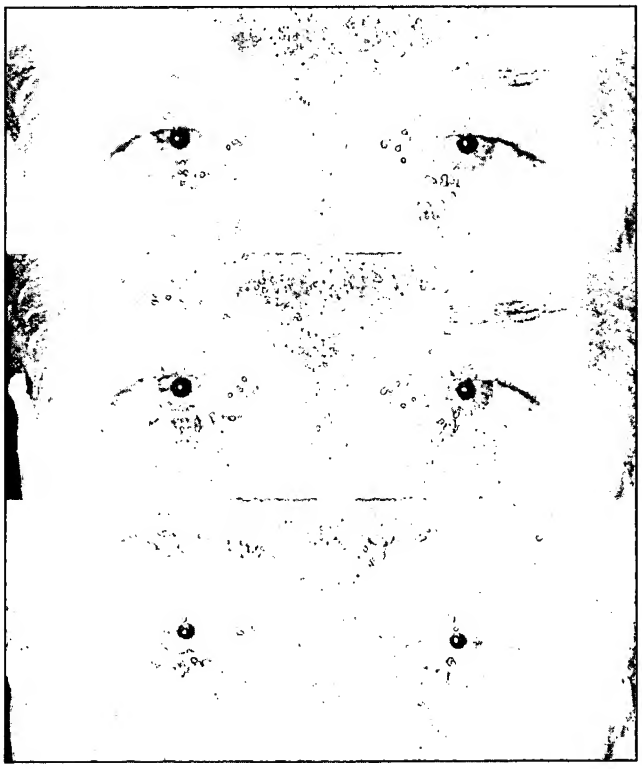

Figure 14. A 52-year-old man. Eyebrow lift with Titan. Pretreatment (upper), immediate (center), and 7 months (lower). Prior treatment with ThermaCool 8 months earlier had been unsuccessful.

Why lower fluences are more effective than higher fluences is not clear. This has been my personal observation with the NARF device as well. One explanation is that heating of the dermis at these energy levels approaches the point of collagen contraction, which is 57 to 61°C. Heating the collagen to a higher temperature may liquefy collagen beyond any possible immediate contraction. The denatured collagen must then be removed by a wound-healing process that in itself would cause tissue contraction but not in an immediate way. A longer pulse also accounts for much less pain during treatment.

When immediate contraction is obtained, the degree of patient satisfaction is remarkable. Immediate gratification is experienced by both the patient and the physician, while the low to moderate

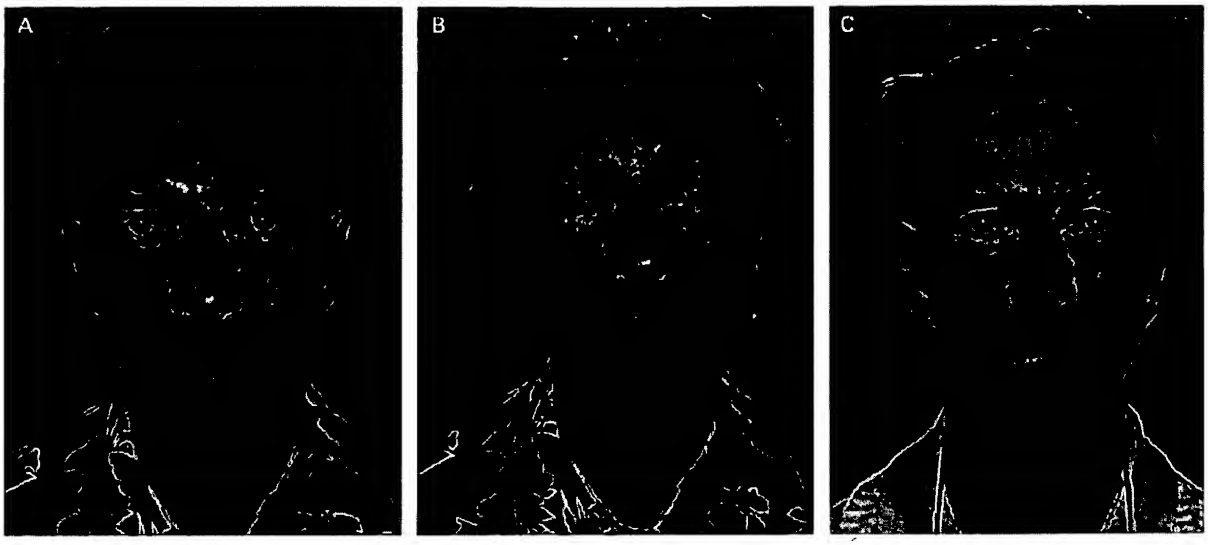

Figure 15. A 68-year-old woman. Pretreatment (A) and immediately after (B) 30 J/cm^3. Notice jowl improvement. (C) One year after a single treatment.

nature of pain during the procedure makes for a much more pleasant experience for the patient and the doctor as well. The need to wait for an hour or two while the topical anesthetic takes effect before the procedure can be started is obviated. This also contributes to improved patient satisfaction.

Acknowledgments The author wishes to express his gratitude and appreciation to Robert Shine, PhD, Director of Marketing, Cutera, Inc. and to Gregory John Roy Spooner, PhD, Staff Optical Scientist, Cutera, Inc. for their valuable input in the technical aspects of the preparation of this manuscript.

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EXHIBIT C

Nonablative Infrared Skin Tightening in Type IV to V Asian Skin: A Prospective Clinical Study

SZE-HON CHUA, FRCP (EDIN),* POR ANG, MRCP (UK),† LAWRENCE S. W. KHOO, MRCP (UK),† AND CHEE-LEOK GOH, FRCP (EDIN)*

BACKGROUND Nonablative skin tightening devices have been developed to treat facial and neck skin laxity without damage to the epidermis. There are at present two main approaches: the pioneer method by monopolar radiofrequency and the second by infrared light.

OBJECTIVE This study aims to determine the clinical efficacy and safety of nonablative infrared light in the treatment of facial and neck skin laxity in Type IV to V Asian skin.

METHODS This is a prospective noncomparative open study. Adult patients with facial and neck skin laxity were recruited for the study. Three treatment sessions spaced 4 weeks apart were performed. Photographic documentation was performed serially during the study period. Final clinical assessment was performed 6 months after the last treatment. Response parameters included patient self-assessment as well as doctor's assessment.

RESULTS Twenty-one patients were evaluated. All patients were of Fitzpatrick skin types IV and V. Patient assessments of response at 6 months after treatment were as follows: 19% reported mild improvement, 38% reported moderate improvement, and 43% reported good improvement. Doctor's assessments of photographs before and 6 months after treatment showed observable lifting of sagging skin folds in 86% of patients. Of these, 28% were assessed as significant-mild, 38% as significant-moderate, and 19% as significant-excellent. The treatments were associated with minimal pain and edema. The main side effect was isolated superficial blistering in 7 episodes of 63 treatments performed, which resolved without scarring in all patients.

CONCLUSION Direct application of infrared light with epidermal cooling is effective in achieving mild to moderate gradual clinical improvement in the treatment of facial and neck skin laxity. The procedure is associated with minimal downtime and is safe for use in darker skin, Types IV and V.

The Titan device used in this study was loaned by Cutera, Inc.

Nonablative treatment of skin laxity has recently been made possible by devices that create uniform heating of the dermis and the underlying tissue. Heating of the collagen to critical temperatures causes the collagen to contract; this process provides the initial results of tighter looking skin soon after the procedure is performed. Subsequent to the initial effect, the skin starts a wound healing response resulting in the formation of new collagen, which provides longer-term tightening of the skin. As a result of these two processes, the skin is tightened, laxity is reduced, and facial contours are renewed.

There are different approaches to heating up the dermis to effect clinical skin tightening. The first is by radiofrequency energy and the second by infrared light. Both these approaches are nonablative and do not require any surgical incision to be made to the skin.

In this study, we evaluate the clinical efficacy and safety of direct application of nonablative infrared light to facial and neck skin to treat facial and neck laxity. Secondary benefits such as improvement in fine lines, reduction in pore size, and improvement in skin texture are also evaluated.

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 • Published by Blackwell Publishing •
ISSN: 1076-0512 • Dermatol Surg 2007;33:146–151 • DOI: 10.1111/j.1524-4725.2006.33032.x

Materials and Methods

This is a prospective noncomparative open study. Twenty-one patients with facial and/or neck skin laxity were enrolled into the study. All patients were of Fitzpatrick skin types IV and V. There were 20 women and 1 man. Patient ages ranged from 43 to 60 years (mean, 52 years). The study protocol conformed to the hospital's ethical guidelines and complied with the 1975 Declaration of Helsinki, and all patients gave informed consent. Inclusion criteria included patients with clinical facial or neck skin laxity who were of legal age (> 21 years) to give informed consent. Exclusion criteria were previous surgery to correct facial skin laxity, recent or previous treatment with radiofrequency skin-tightening devices, pregnancy, isotretinoin use over the past 12 months, photosensitizing drugs such as tetracyclines, aspirin, anticoagulants, active wound infections, vitiligo, and history of keloids.

Patients were treated with an infrared nonablative heating device (Titan, Cutera, Inc., Brisbane, CA). The integrated handpiece of the device incorporates contact epidermal cooling before, during, and after the heating phase of each treatment exposure.

Topical anesthesia using topical anesthetic cream (EMLA, AstraZeneca, London, UK) under occlusion for 1 hour of pretreatment was given to minimize patient discomfort. Treatment areas were then thoroughly cleansed of the topical anesthesia and makeup. A layer of refrigerated ultrasound gel, 1 mm thick, was applied to the entire treatment area. For the cheeks and jowls, the treatment area comprised the entire cheek from 10 mm below the lower border of the lower eyelid to the edge of the mandible. For the anterior neck, the treatment area was from the midneck up to the edge of the mandible.

Three passes of adjacent nonoverlapping exposures were made over the treatment areas. The following treatment parameters were used: 32 to 40 J/cm^2 over the soft tissue of cheeks and submental area and reduced fluence of 28 to 32 J/cm^2 over bony areas and forehead. Each exposure consisted of sequential precooling, heating, and postcooling whose timings were preprogrammed. The entire treatment areas were treated before the next pass was administered, and duration between each pass was approximately 15 to 20 minutes. Attention was paid to ensure proper contact of the treatment window measuring 1.5 × 1 cm throughout the treatment exposure of precooling, heating, and postcooling. No routine posttreatment was necessary. Patients were advised to avoid unnecessary sun exposure and tanning during the peritreatment period. A total of three repeated treatments were carried out at monthly intervals.

Before each treatment, patients were questioned on the effects from the previous treatment. Patients were asked to assess the degree of skin tightening subjectively, and possible side effects were recorded. Photographic documentation was performed before each treatment and 3 and 6 months after the last treatment.

Final assessment was performed 6 months after the last treatment. Response parameters included patient self-assessment of skin tightening as well as doctor's assessment. Patient's self-assessment was obtained by recording the subjective degree of skin tightening after treatment compared with before treatment. Patient assessment included feeling of increase in skin firmness and tone as well as observable lifting of sagging skin. Improvement was recorded by patients as none, mild, moderate, and good.

Doctor's assessment was based on the evaluation of pre- and posttreatment photographs by three independent dermatologists who were not part of the study. Photographic assessment of skin tightening focused on assessing observable lifting of skin folds such as the nasolabial folds and marionette lines, renewing of contours along the jaw, and lifting of submental sagging skin. Improvement was assessed by doctors as none, significant-mild, significant-moderate, and significant-excellent.

Secondary response parameters such as effects on skin texture, pore size, and fine lines as reported by patients were also recorded. These parameters were assessed by direct questioning of the patients after each treatment in the form of structured questionnaire in which patients were asked to rate each parameter as being worse, no change, or improved after treatment as compared with before treatment.

Results

All 21 patients completed the treatments and follow-ups; none dropped out of the study because they were unable to tolerate the treatment or side effects. During all treatments, patients felt only minimal or no pain. No patient felt severe pain requiring additional pain relief with analgesia or sedation.

Patient assessments of response at 3 months after treatment were as follows: 5% reported no improvement, 38% reported mild improvement, 33% reported moderate improvement, and 24% reported good improvement. At the final 6-month posttreatment, patients' reports were as follows: 0% reported no improvement, 19% reported mild improvement, 38% reported moderate improvement, and 43% reported good improvement (Figure 1). Seventy-five percent of patient reported that they were quite satisfied to very satisfied with the treatment results, 20% of patients were just a little satisfied, and 5% of patients were not satisfied.

Figure 1. Patient self-assessment of skin tightening.

Doctor's assessment of photographs before and 6 months after treatment showed observable lifting of sagging skin folds in 86% of patients. Of these, 29% were assessed as significant-mild, 38% as significant-moderate, and 19% as significant-excellent (Figures 2–5). Secondary benefits reported by patients at 6-month posttreatment included improvement in skin texture (60%), reduction in pore size (50%), and reduction in fine wrinkles (40%).

Complications

Of the 63 treatments that were performed, there were 7 minor episodes of superficial blistering. These blistering episodes occurred in the early phase of the study when higher fluences (36–40 J/cm^2) in the treatment parameter range were used. None occurred when lower fluences (28–34 J/cm^2) were used in subsequent treatments. All these resolved with temporary postinflammatory hyperpigmentation. At the final 6-month posttreatment review, no scarring or residual dyspigmentation was present. No significant pain or edema was noted during or immediately after the treatment.

Discussion

Nonablative treatment of skin laxity has recently been made possible by devices that are able to deliver uniform heat deep into the dermis while preserving epidermal integrity by effective surface cooling. This heating process causes initial collagen contraction which may be noticed soon after the procedure as immediate skin tightening.[1] Although the initial tightening may be impressive to patients, it is often temporary. More importantly, the heating initiates progressive collagen remodeling over the next several weeks and months resulting in gradual skin tightening and reduction of skin laxity.[1]

There are currently two approaches to the delivery of heat. The first is by radiofrequency energy. Monopolar radiofrequency devices were the first to be reported in scientific literature to be able to produce clinical skin tightening without causing epidermal

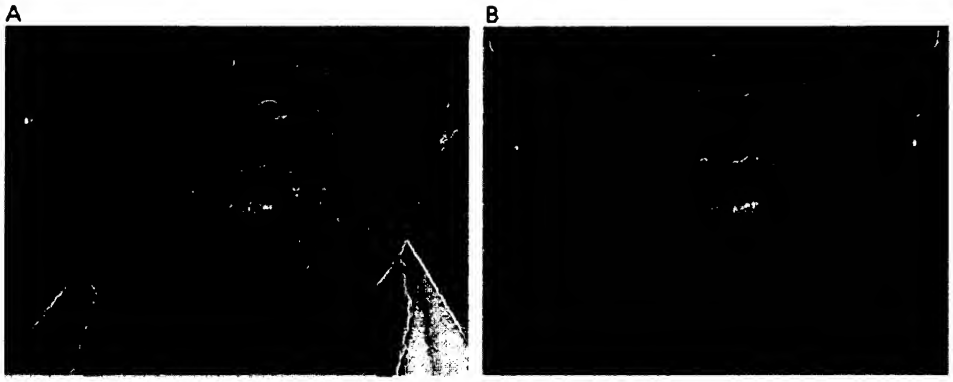

Figure 2. Before (A) and after (B) pictures showing significant improvement in mid and lower facial laxity 6 months after three infrared treatments.

damage.[2] To date, there have been several articles demonstrating the efficacy of monopolar radiofrequency skin-tightening devices.[2–5] Initial protocols using single-pass high-energy settings were associated with higher incidences of side effects such as erythema, edema, blistering, and subcutaneous fat necrosis. Subsequent reports suggest that using multiple passes with lower-energy settings are probably safer, more tolerable, and efficacious.[5,6] Multiple treatments also tended to give better results than a single treatment.[7,8] In darker Asian skin, monopolar radiofrequency has been shown to be effective as well in treating facial skin laxity.[9]

An alternative approach to delivering uniform heat deep into the dermis is via direct application of nonablative infrared heat as evaluated by this study. The device used in this study emits a broadband light spectrum between 1,100 and 1,800 nm. Epidermal protection is effected by integrated contact cooling before, during, and after the heating phase of each exposure. Following lessons learned from radiofrequency skin tightening, multiple passes using moderate fluence were employed in this study to maximize safety and efficacy. Three treatments performed monthly were done again to maximize clinical outcomes and to demonstrate efficacy if present. The results of this study demonstrated that infrared light is able to treat skin laxity of the face and neck. Results are, however, gradual and subtle with photographic assessments showing significant improvements in 86% of patients. Results at 6 months appear superior to that at 3 months according to patient assessment data consistent with the

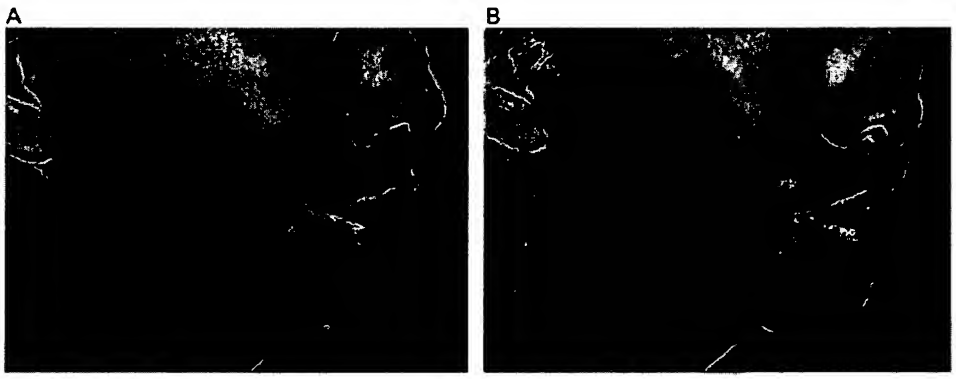

Figure 3. Before (A) and after (B) pictures showing significant improvement in mid, lower facial and upper neck laxity 6 months after three infrared treatments. The clinical improvements are clearly evident despite mild variation in the lighting/exposure between the two pictures.

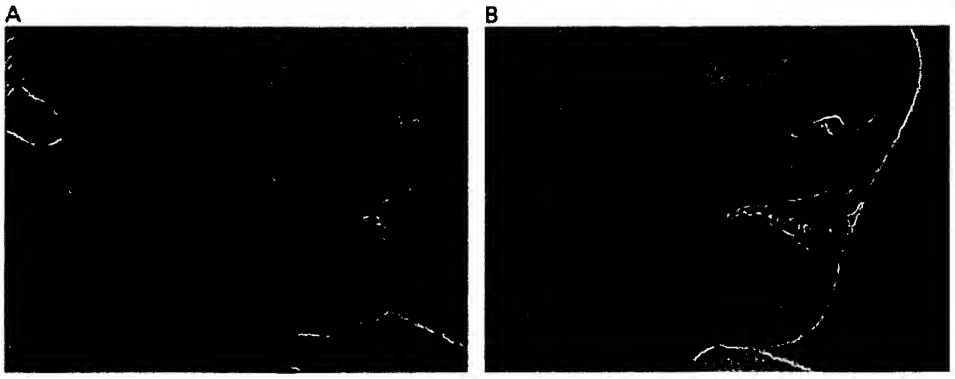

Figure 4. Before (A) and after (B) pictures showing significant improvement in mid and lower facial laxity 6 months after three infrared treatments.

progressive collagen remodeling that occurs as part of the healing process. The close age range of our patients (20/21 were between the ages of 50 and 60) did not allow us to analyze clinical response relative to age groups; it is, however, likely that younger patients with less advanced skin laxity and who are not obese will demonstrate better clinical response.

The relative merits of radiofrequency and infrared approaches remain to be clarified. Taking previous reports in the literature into consideration, the infrared approach appears to be less painful and is associated with minimal/no local edema; although new and revised monopolar radiofrequency technologies utilize lower energy and are also associated with less pain. Superficial blistering is a problem when high fluences are used, and a lower fluence (28–34 J/cm^2) is recommended when treating Asian facial skin. The incidence of blistering can also be reduced by ensuring proper contact of the treatment window to the skin during exposures and by ensuring an interval of at least 5 minutes between each treatment pass.

Our study also demonstrated that subjective improvements in skin texture and pore size were reported by patients although these improvements were not validated by objective measurements. As such, we hesitate to recommend this treatment for these complaints until objective and sustainable results can be demonstrated by further studies.

In conclusion, our study demonstrates that the nonablative infrared light with integrated epidermal cooling is effective in the treatment of facial and

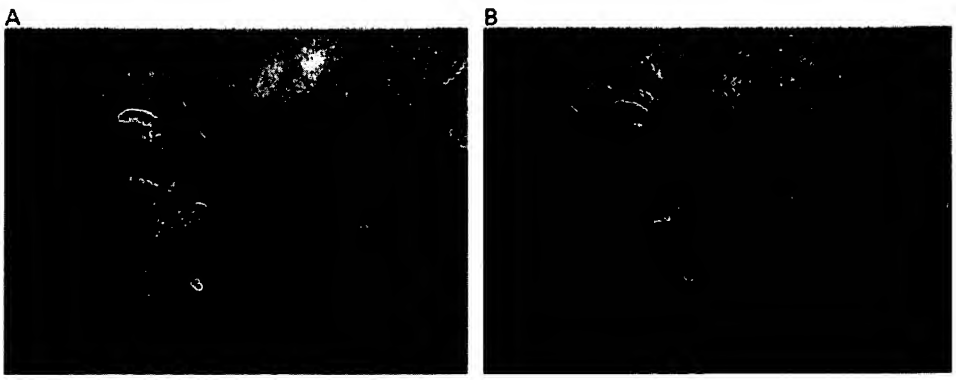

Figure 5. Before (A) and after (B) pictures showing significant improvement in the nasolabial folds 6 months after three infrared treatments. The clinical improvements are clearly evident despite mild variation in the lighting/exposure between the two pictures.

neck skin laxity. Results are, however, gradual and variable with observable clinical improvement achievable in 86% of patients. The infrared approach is a viable alternative to the pioneer radiofrequency approach in the nonablative treatment of facial skin laxity. The findings of our study will be useful for physicians using this new modality in treating patients with darker skin types in their community.

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EXHIBIT D

Multicenter Clinical Perspectives on a Broadband Infrared Light Device for Skin Tightening

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Abstract

Modalities for skin tightening include radiofrequency (RF) energy, lasers, and combination RF and diode lasers. A new broadband infrared light device (BILD) (Titan, Cutera, Inc, Brisbane, CA) targets water to achieve dermal heating and collagen remodeling for skin tightening. Although thousands of procedures have been performed worldwide with this device, only one article (to the author's knowledge) describing its performance in skin tightening has been published.

Three US dermatologists report their experience with and provide their perspective on facial skin tightening with the BILD system. As early adopters, they each have 12 to 18 months experience with this system. One author (A.F.T.) treated 42 patients twice at 1-month intervals over 18 months. The mean improvement score was 1.83 (scale 0 to 4, with 4 denoting maximum improvement) with an average follow-up time of 3.7 months. More than 90% of treated patients showed visible improvement. No complications were observed and patient satisfaction was high.

This paper presents the general consensus of the authors on patient selection and treatment protocol, their modifications of the manufacturer's treatment protocol, and the outcomes of 42 patients treated by one author (A.F.T.). The observations were gathered separately and turned out to be very similar. The recommendations are presented to help practitioners achieve consistently good results and avoid complications with the BILD procedure.

Introduction

With the advent of nonablative rejuvenating devices, dermal fillers, and botulinum toxin, there is a general understanding that the 3-dimensional framework of the aging face can be altered in a nonsurgical way that creates a more youthful appearance. This has led to an increased interest in tissue tightening procedures.

The idea of bulk dermal heating for collagen contraction and synthesis yielding nonsurgical 3-dimensional improvements is relatively recent.[1] Tissue tightening with noninvasive technology was originally pioneered in a device that uses radiofrequency (RF) to heat tissue by electrical impedance.[2-4] Other modalities for skin tightening include lasers,[5,6] and combined RF and diode laser.[7] A new broadband infrared light device (BILD) was created to utilize water as a chromophore to achieve dermal heating and subsequent collagen remodeling.[8] The profile of dermal heating is targeted at the 1 to 2 mm depth[8] whereas the RF device targets tissue at 3 to 4 mm in depth.[9]

There is only one published article on the BILD procedure,[8] despite the thousands of treatments that have been performed in the past 2 years worldwide. Initial treatments with the RF (Thermacool, Thermage, Inc.) device had initial well-publicized complications[10] as well as modest results due to the fact that it wasn't understood initially that lower fluence, multipass treatments were superior both in efficacy and safety.[11,12] Early adopters of this new infrared technology have had the advantage of prior knowledge of the multipass-low fluence technique.

Three US dermatologists report their experience with and provide their perspective on skin tightening of the face with the BILD system. They are among the earliest adopters and each has 12 to 18 months experience with the system. This paper presents their general consensus on patient selection and treatment protocol as well as their individual modifications of the manufacturer's treatment protocol. These observations were gathered separately but turned out to be very similar. They are presented to help practitioners achieve consistently good results and avoid complications.

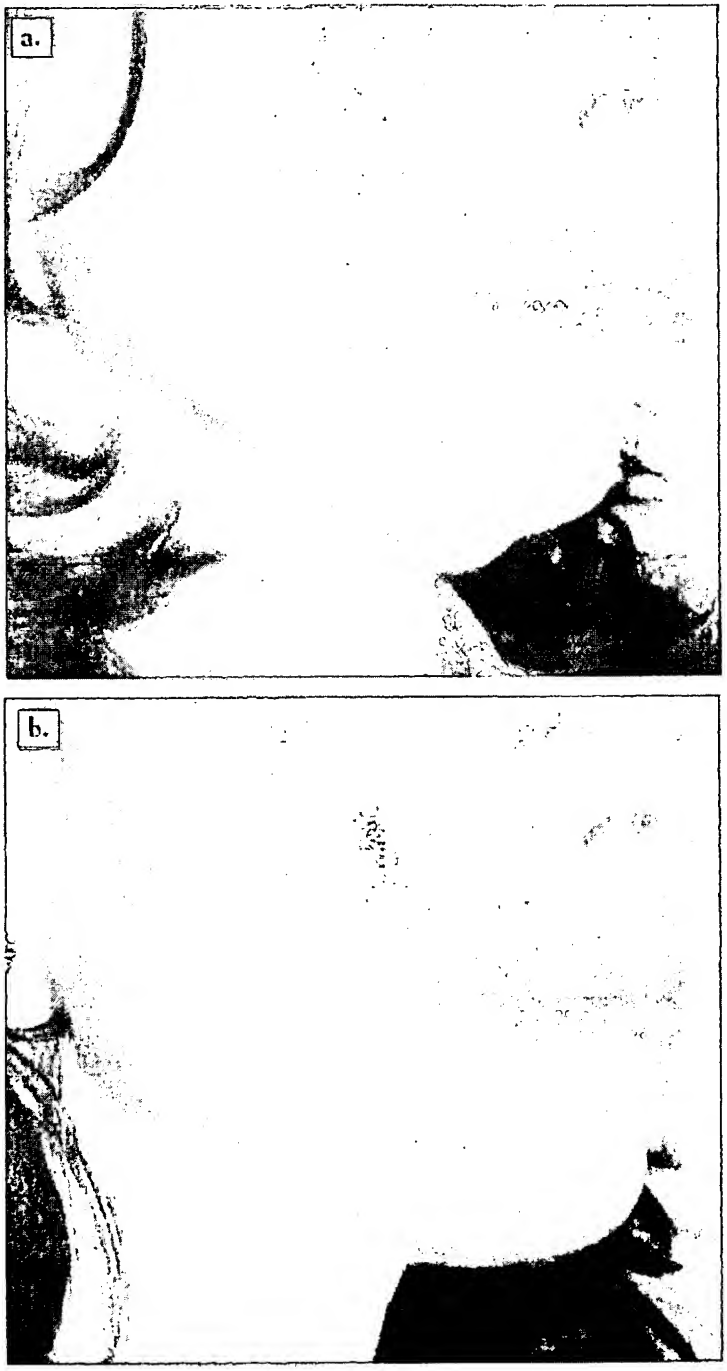
One author (A.F.T.) analyzed outcomes of patients that received this procedure in her practice up to the current date. Treatment protocols and outcomes are presented in detail.

Patient Consultation and Selection

It is important that patients have realistic expectations as well as the ability to document the changes with treatment. The majority of patients want their faces, especially jowls and necks tightened (Figure 1). Patients in their late thirties notice their malar skin beginning to descend into the nasolabial folds. Those in their forties complain of jowling and loss of definition along their jaw line. Patients in their forties and fifties may have cheek descent, jowls, and submental laxity with or without a submental fat pad. Those in their sixties may be candidates for laser resurfacing or surgical lift to redrape redundant skin.

The best responders to BILD treatment have early changes along the jaw line or malar area and in thin submental skin with minimal fat to support. Neck skin, often being thinner than facial skin, can be an ideal target. Skin laxity that is

Figure 1. a) Lower right side of the neck of a woman before treatment. b) Improvement in neck laxity 6 months after the final of 3 treatments with the BILD. Photograph courtesy of Eliot F. Battle Jr. MD.



more a result of sagging and dermatochalasis, and less due to subcutaneous fat volume weighing the area down, seems to respond best to the BILD procedure. Results are achievable but less reproducible when subcutaneous tissue is voluminous, or skin is relatively thick and/or sebaceous.

Age and illness may play a role. Collagen synthesis is more sluggish and collagen breakdown not as well-defended against in patients who are older.[11] We have noticed in a couple of patients over 65 there may be a drop-off of results after 9 months to a year, unlike that of younger patients. In addition, diabetes and/or recent chemotherapy, smoking, excessive sun exposure, collagen vascular disease, radiation, or prolonged illness may also be factors for less optimal results. Although there is no absolute contraindication, it would be best to counsel these patients that they may require more treatments and more maintenance and achieve less improvement than those without any metabolic deficiency.

As with all cosmetic procedures, management of patient expectations is a top priority. Patients must realize that, while some degree of skin tightening is immediate,[2] much of the result is delayed. Also, results can be noticeable but subtle. Although good results can be noted as early as one month, 4 to 6 months is a more optimal time to view before and after photographs. Because the changes are gradual and the patient sees themselves in the mirror every day, they often need to see their before and after picture side by side to appreciate the changes. We also suggest combining the BILD procedure with complementary therapies to achieve maximum benefit.

For the outcome study, all included patients had been treated with BILD over the course of 2 years in a private cosmetically oriented dermatology practice. Patients were excluded from the evaluation if they had less than 2 treatments (a single treatment was determined to be inadequate), or if they had had any other tissue tightening procedures within a year or fillers or botulinum toxin (due to confounding variables).

Treatment Protocol

Most practitioners do more than one treatment separated by 1- to 3-month intervals. Those who argue for earlier repetition think that it may be beneficial to stimulate collagen before it settles down from the previous treatment. A 2- to 3-month interval may allow more complete formation of new collagen through the wound-healing response. Improvement usually continues for 3 to 6 months after treatment. We recommend follow-up visits at 2- or 3-month intervals (or up to 6 months) posttreatment to assess the ultimate outcome.

The general treatment begins with 1 to 2 complete passes over the targeted area. The basic treatment plan involves identifying areas that have redundant or overabundant skin (such as at the jowls or submental fat pad) and the "vectors" of lifting. Vectors can be determined by pulling on the skin with the second and third fingers in the direction of correction desired and finding the best location of "pull." These are the areas to place "vectors" or "focused" passes. For overabundant skin, multiple and/or stacking pulses *directly* over the area to be shrunk is advised, whereas for a lifting effect, multiple passes should be done to the vector, or the areas where the fingers are placed that yield maximum improvement on skin manipulation. Fluences should be obtained that yield a warm to hot sensation for the patient but are not so uncomfortable that they want to withdraw from the pulses. For more experienced practitioners who wish to use higher energies, a topical anesthetic may be used. This

may result in a higher risk of complications and, therefore, should only be undertaken with expert knowledge of the procedure. The consensus recommendations of the 3 participating physicians are shown in Tables 1 and 2.

Results

While not a substitute for a facelift, the BILD procedure noticeably improves skin laxity. Response varies among patients. In 85% to 90%, there was mild to moderate improvement 1 to 3 months after the second BILD treatment. The degree of improvement is consistent with the 20% to 30% collagen contraction and secondary collagen remodeling previously reported.[11] Tightening continues for several months and stabilizes after 4 to 8 months (Figure 2).

Overall results are relative to age. BILD treatment has the greatest impact in patients with less laxity to reverse (usually younger patients, Figures 1 and 3) but older patients see visible correction as well (Figure 4).

The types of beneficial results that are common with BILD include reduction of jowling and improved definition of the jawline (Figure 5), tightening of the upper cheek with reduction of laxity, narrowing of the face into an oval effect that improves the squaring phenomenon common in middle age, brightening of the skin and improvement in more superficial wrinkles, reduction in the nasolabial fold, reduction of skin laxity and submental excessive fat pad. Brow elevation can be achieved with forehead and temple area treatment. Prominent platysmal bands can lessen the visual impact of skin tightening on the neck.

Patient satisfaction, while not the only way to measure results, is perhaps the best method. Patients are generally happy with correction and say they are willing to return for a yearly or every other year touch-up. Combining BILD with other treatments (eg, botulinum toxin, dermal fillers) enhances the overall effect and improves the likelihood of patient satisfaction (Figure 6). Pre- and posttreatment photographs are essential because they remind patients of their pretreatment laxity and highlight more subtle improvements achieved by treatment.

One author (A.F.T.) collected detailed data on all patients who received BILD treatments in her practice for the first 14 months. Outcome data for 42 treated patients are presented in Table 3. Patients were excluded if lost to follow-up, had received dermal fillers or botulinum toxin, or had previous treatment with RF or a combination of RF and optical energy.

For the patient population that was studied in detail (A.F.T.), all patients received at least 2 treatments with only one having more. Protocols were similar to those outlined above, with 2 full passes and usually 4 to 8 "sculpting" or vector passes at fluences in the 30 to 38 J/cm^2 range, with the average being 34 to 36 J/cm^2 and an average of 150 to 250 pulses per treatment. High-definition serial photography (Canfield VISIA CR system) was utilized to evaluate results.

Patients were treated on the face, neck, or combination of these areas. One patient (=13) was treated on the abdomen as well as the lower face and neck. All patients received 2 treatments spaced approximately 1 month apart; one patient received 3 treatments. Protocols were similar to those in Table 2, with 2 full passes and 4 to 8 "sculpting" or vector passes at 30 to 38 J/cm^2 (average 34-36 J/cm^2) and 150 to 250 pulses (average) per treatment. The mean follow-up time was 3.72 months (2.85-4.60, 95% CI). Improvement was graded on the following scale: none = 0 (0%); mild = 1 (1%-25%); moderate = 2 (26%-50%); marked = 3 (51%-75%); outstanding = 4 (76%-100%).

Table 1. General Treatment Protocol Consensus.

Treatment Area	Fluence Target Range (J/cm^2),* Total Pulses	No. & Types of Passes	Endpoints
Lower 2/3 of face *(50 min)*†	32-38,‡ 200-250	1-2 complete passes, 2 direct passes on supramandibular area, 1-5 focused passes§ or 4-8 vector passes to tighten skin	Visible and palpable firming and tightening in desired areas
Forehead *(15 minutes)*	30-36, 100¶	2 complete passes, 2-6 vector passes on brow along desired vectors of lift	Visible and palpable firming and tightening in desired areas
Neck *(30 minutes)*	30-36, 150#	2 complete passes, 2 focused passes§ or 6-8 vector passes on submentum and lateral neck	Visible and palpable firming and tightening in desired areas
Upper Chest *(30 minutes)*	34-38, 200	2 complete passes	Visible and palpable firming and tightening in desired areas
Abdomen (variable: 50-90 minutes)	34-40, variable	2 passes encompassing involved area and vectors, 6-8 sculpting passes	Visible and palpable firming and tightening in desired areas and umbilicus definition

*Start at low end of range and increase, adjusting to tolerance.
†Application of topical anesthetics such as benzocaine/lidocaine/tetracaine (BLT) may increase time to 90 min.
‡May need to reduce fluence by 2 over nasolabial fold.
§Refers to placement either along vector lines or directly on area to be flattened.
¶Treat temple at 30-32 J/cm^2.
#Maximum 100 pulses for anterior neck.

Table 2. Treatment Tips and Variations.

General Treatment	1) Treat one side at a time to achieve and maintain a critical mass of heat and to more easily appreciate the changes by comparing them to the contralateral side. Constantly pull the tissue to feel if it is decreasing in laxity and if you are on the right vector. 2) To diminish bulky areas (eg, nasolabial folds, submandibular fat pad) stack 1 to 3 passes directly onto the involved area; take care not to overheat the skin. 3) After treating one half of the face, photograph and show the patient the immediate results before treating the second half. 4) To determine spot placement for vector passes, gently manipulate the skin to determine laxity and "drawstring" areas of lift.
Facial Sculpting	1) Perform a single complete pass to warmth (but no discomfort) for collagen enhancement, then focused passes on problem areas. 2) Perform 2 arch "L" passes: 2 rows beginning on the temple, down the lateral cheek/pre-auricular area, and across just above the mandible, plus one row just below the mandible. To avoid further loss of volume or concavity, exclude thin skin over midcheek. 3) Use the highest tolerable fluence, but if pain becomes too great reduce the fluence to a much lower level (30-32 J/cm^2) and increase the number of passes to five or six. 4) Application of topical anesthetics such as benzocaine/lidocaine/tetracaine (BLT) cream (30 minutes, then remove) allows the use of higher fluences (38-40 J/cm^2), but this increases the treatment time to 90 minutes. Reapply cream to individual sections immediately before placing pulses. It also reduces the value of patient feedback regarding discomfort and increases the risk of overheating the skin. 5) Treat to visible tightening or maximum passes.
Neck Sculpting	1) Determine placement of the tip by pulling on the skin with 2 fingers and observing which area yields the most tissue movement. Do more passes in which your fingers are acting as vectors. 2) Start one row above the mandible from chin to bottom of the ear, then diagonally down to the collarbone 2/3 from midline and across to the sternal notch. Fill in with rows up to the chin, avoiding the prominentia laryngea.

Figure 2. a) Patient before treatment. b) Patient 3 months after final treatment; patient had received a single radiofrequency (Thermage) treatment on the left side of the face and 2 BILD treatments on right side. c) Eight months after final treatment, showing that long-term follow-up often reveals even greater improvement and improvement on both sides was similar. Photographs courtesy of Amy Forman Taub, MD.

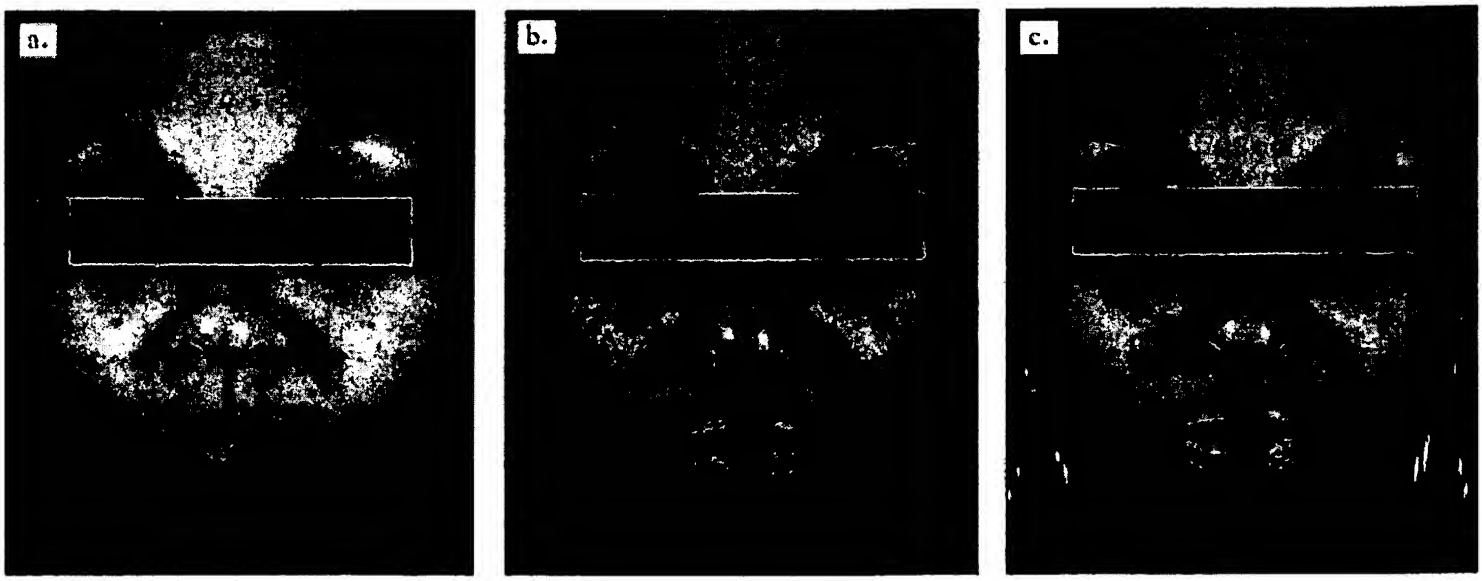
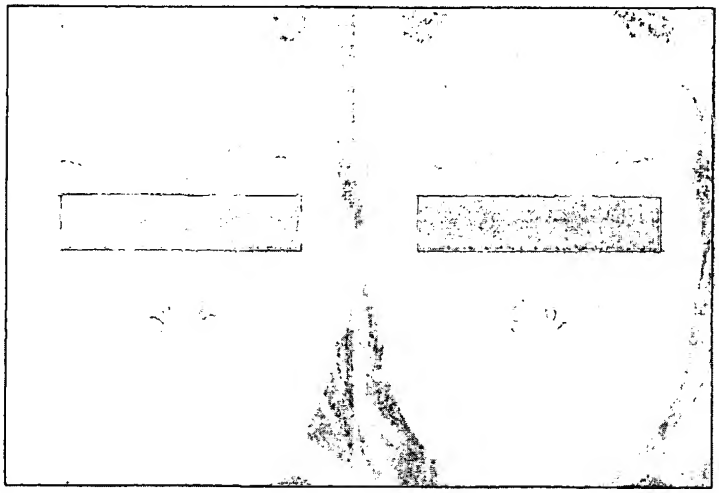


Figure 3. (Left) A younger woman before treatment. (Right) Improvement in skin laxity 3 months after 2 treatments with the BILD. Photographs courtesy of Amy Forman Taub, MD.



Thirty-eight of the 42 patients (91.75%) had visible improvement. Improvement was outstanding in 1 patient, (Figure 6), moderate in 14, mild in 16, and not visible in 4. Improvement was moderate or better in 22 patients (52.4%). No response was seen in 4 patients (9.25%). The mean improvement score was 1.83 (1.43-2.34, 95% CI). In patient #13, improvement in the abdomen was marked (51%-75%) at the 1.5-month follow-up evaluation (not included in the statistics). Twenty patients had less than 3 months follow-up. This means that if there had been longer term follow-up, the results would very likely have been even better, as we have noted an increasing improvement in many patients for up to 8 months. Improvement in the lower face after BILD treatment is shown in Figures 4 and 5.

Complications

The main complications of nonablative rejuvenation procedures are the same that we see with the BILD. Minor swelling and erythema, which is usually short-lived (a few hours), can occasionally last for a couple of days. Discomfort

Figure 4. a) An older woman before treatment. b) Improvement in facial skin laxity 2 months after 2 treatments with the BILD. c) Neck of same woman before treatment. d) Neck after 2 treatments with the BILD. Photographs courtesy of Amy Forman Taub, MD.

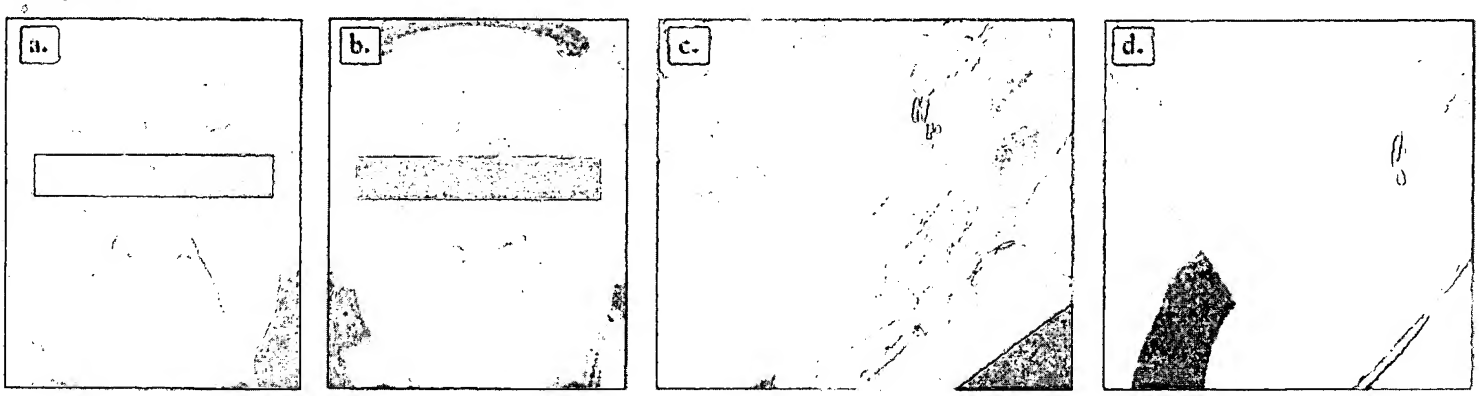
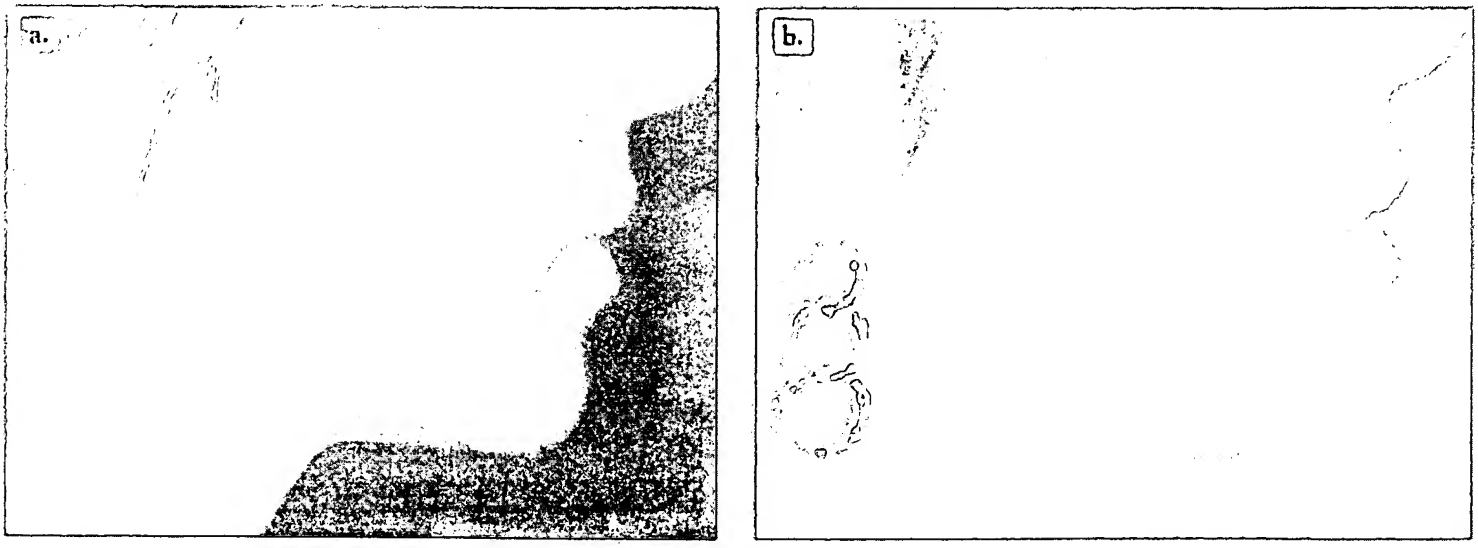


Figure 5. a) Lower right side of face and neck of 58-year-old woman before treatment. b) Improvement in skin laxity 1 day after a single treatment with the BILD. Photographs courtesy of Gregory Nikolaidis, MD



with the procedure is expected but is tolerable and doesn't last after completion of the treatment. The most common significant adverse effect is overheating of the skin which can lead to blistering, and potentially dyspigmentation and/or permanent scarring. These 3 doctors have done over 1,000 treatments in the past 1.5 years and only report 2 blisters, neither of which caused permanent sequelae.

One author (G.N.) has treated approximately 200 patients. Adverse effects have been limited to immediate blistering, which occurred in 2 of the first 100 patients treated. No blistering has occurred in the most recent 100 patients, suggesting that blistering is related to technique. No posttreatment complications have been observed in patients up to 18 months after the final of 2 to 3 treatments.

As with all laser or light procedures, proper selection of patients and techniques is important to both the safety and efficacy of the BILD procedure. Used properly, there appears to be an extremely low side effect profile.

Discussion

BILD improvement should be evaluated by considering topical skin products on one end of the spectrum and ablative and/or surgical procedures on the other. The greater improvement achieved with surgery must be weighed against surgery's higher risks and cost. If expectations are managed properly, patients welcome the degree of correction achieved with the BILD. In fact, much of the BILD's appeal is that it is not surgery.

Patient acceptance is important in making the BILD a commonly performed and sought out procedure. The BILD's appeal stems from its positive safety profile, which attracts a new category of cosmetic patients—those considering an elective aesthetic procedure for the first time. These patients are willing to forego the visual impact of surgery for the accessibility and patient-friendliness of the BILD. The consistently high level of satisfaction among patients of all ages increases the referral base over time.

The demand for skin tightening is growing rapidly. The BILD went from being an "experimental" procedure to one that is performed every day in the office (A.F.T.). For another author (E.F.B.), the volume of BILD procedures increased from 5 per week to more than 30 per week during the first year.

Virtually any person aged 30 years or older may be a candidate for skin tightening. The best responders to BILD treatment have early changes along the jaw line and thin submental skin with no fat to support. Patients with a large amount of redundant skin can also benefit, but results are more difficult to achieve when subcutaneous tissue is voluminous, possibly because infrared light penetrates only 1 to 2 mm in depth.

The detailed data from 42 patients in one center revealed that over 90% of patients had a visible improvement after 2 treatments and 3 months of follow-up with no complications. Proper technique and thorough understanding of the volume esthetics of the face is essential to achieving good results.

Figure 6. a) Before treatment. b) Woman 3 months after receiving 2 BILD procedures, botulinum toxin, and hyaluronic acid filler (Restylane). Photographs courtesy of Amy Forman Taub, MD.

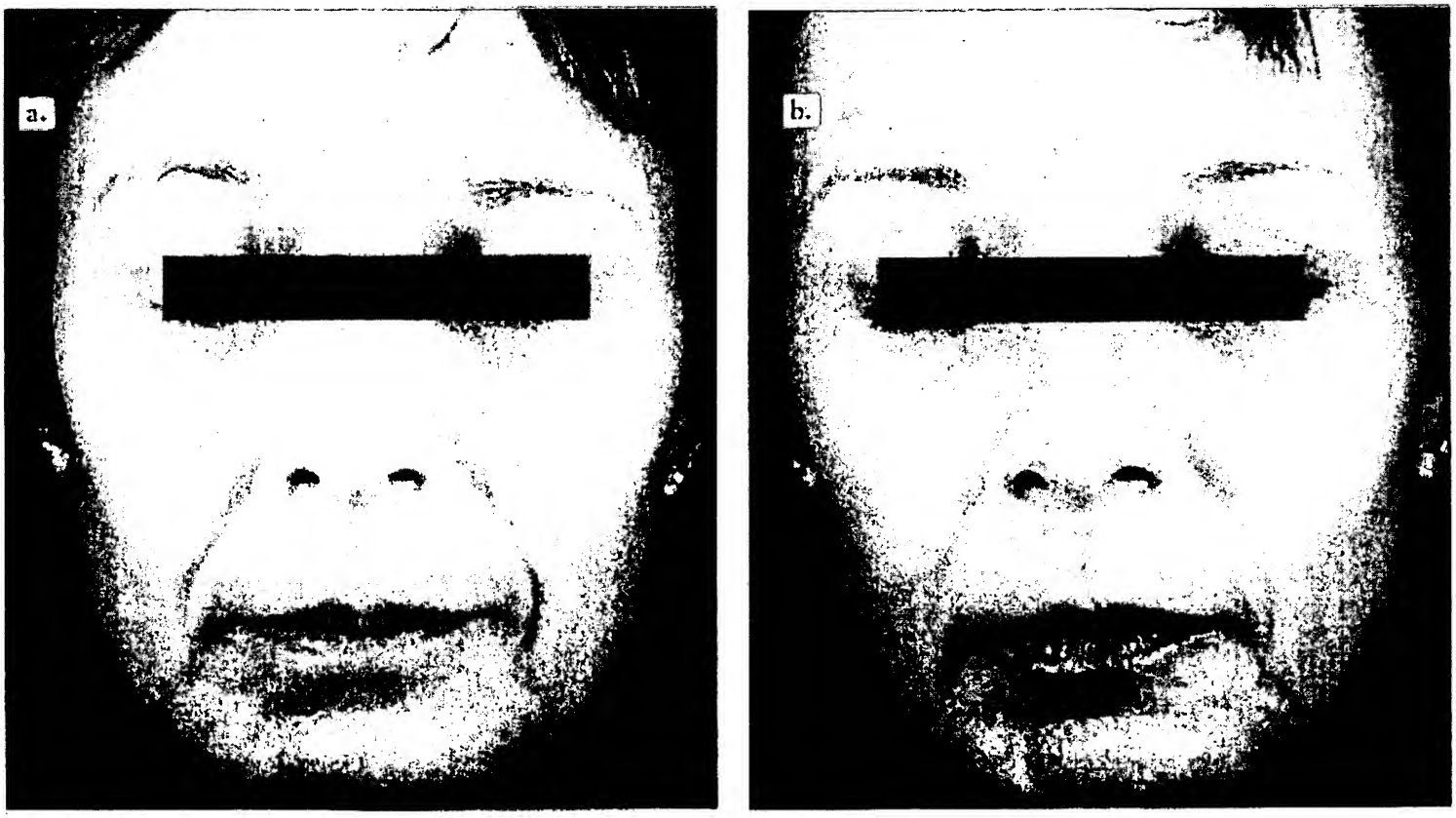


Table 3. Outcomes Data for 42 Patients Treated with the BILD.

Pt #	Area Treated	No. of Tx	Interval (wk)	FU (mo)	Improvement	Improvement Grade*
1	Face	2	4	1.5	Mild	1
2	Lower face/neck	2	4	10	Moderate	2
3	Lower face/neck	2	3	2	Marked	4
4	Full face/neck	2	7	3	Moderate	2
5	Face	2	5	2.7	Moderate	2
6	Jaw/neck	2	4	3.5	Marked	4
7	Face/neck	2	5	14	Moderate	2
8	Face	2	6	0.7	Moderate	2
9	Face	2	4	4	Moderate	2
10	Lower face	2	4	2.2	Mild	1
11	Lower face (nasolabial folds, perioral)	2	4	4	Mild	1
12	Lower face/neck	2	4	2	Mild	1
13	Lower face/neck	2	4	1	Mild	1
13a	Abdomen	2	2.5	1.5	Marked	4
14	Lower face/neck	2	4	3	Mild	1
15	Full face/neck including perioral	2	4	1	Mild	1
16	Lower eye/face	2	5	1	Mild	1
17	Lower face/neck	2	4	7	Mild	1
18	Lower 2/3 face	3	4	4	Moderate	2
19	Lower 2/3 face	2	4	2	Mild	1
20	Face (& abs)	2	4	6	Moderate	2
21	Lower 2/3 face (split face)	2	4	4	Outstanding	5
22	Lower 2/3 face (split face)	2	4	7	Moderate	2
23	Cheeks/glabellar	2	4	9	Mild	1
24	Lower face/neck	2	4	5	None	0
25	Full face & split neck	2	4	6	Mild	1
26	Arms	2	4	3	Marked	4
27	Lower face/neck	2	4	5	Marked	4
28	Lower face	2	4	6	Mild	1
29	Neck (perioral 12/13/05, 2/6/06)	2	4	1	Mild	1
30	Lower face/neck	2	3	2	None	0
31	Lower face/neck	2	4	1	Marked	4
32	Neck	2	4	1	Moderate	2
33	Lower face	2	4	1.5	Marked	4
34	Neck (lower face 11/1/05)	2	4	7	Moderate	2
35	Full face/neck	2	3	1	None	0
36	Face	2	4	5	Moderate	2
37	Lower face	2	5	2	Mild	1
38	Full face/neck	2	3	4	None	0
39	Lower face/neck	2	3	4	Moderate	2
40	Lower face/neck	2	4	2	Moderate	2
41	Lower face	2	4	2.7	Mild	1
42	Face	2	4	2.5	Marked	4

None = 0 (0%); mild = 1 (1-25%); moderate = 2 (26-50%); marked = 3 (51-75%); outstanding = 4 (76-100%).
Tx = treatment

Conclusion

The BILD procedure is safe and effective and has established itself as an integral part of the 3-dimensional rejuvenation of the aging face and neck in these 3 dermatology practices.

Disclosure

Dr. Taub received discounted prices for equipment purchased from Cutera and honoraria from Cutera for educational and marketing activities. Cutera provided financial support for manuscript preparation, including statistical analyses, but did not provide any funds for participation in this study. Dr. Battle received discounted prices for equipment purchased from Cutera and honoraria from Cutera for educational activities.

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